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FROM THE ALLERGY DIVISION OF THE JEWISH HOSPITAL OF BROOKLYN

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ASTHMA AND HAY FEVER

Cardiopulmonary Function in Bronchial Asthma: A Comparison With Chronic Pulmonary Emphysema. Williams, M. H., and Zohman, L. R.: Am. Rev. Res. Dis. **81**: 173, 1960.

A study was made to determine the type and degree of abnormality of cardiopulmonary function present in 15 patients with bronchial asthma. The question as to whether or not pulmonary function in asthmatic patients with chronic dyspnea differs from that in patients with chronic obstructive emphysema was also investigated. These patients gave a history of attacks of wheezing and acute dyspnea precipitated by known allergens or respiratory infections and relieved by bronchial dilators. Measurements were made of ventilatory function, arterial blood gas composition, diffusing capacity, and pulmonary circulation. These studies showed mild hypoxia and carbon dioxide retention which were only slightly increased during muscular exercise. The exercise diffusing capacity was subnormal in most of these patients but always above 11 c.c. per minute per millimeter of mercury. There was minimal pulmonary hypertension at rest and a decided increase of the pulmonary arterial pressure during exercise. The cardiac index was normal or elevated at rest for the degree of oxygen consumption measured and normal or reduced during exercise. As a group the patients with asthma revealed less impairment and greater variability of ventilatory function than patients with emphysema. Moreover they showed greater improvement after the administration of bronchial dilators. The impairment of arterial blood gas composition was slightly greater in emphysema than in asthma, the degree of pulmonary hypertension during exercise was similar in the two groups and the cardiac output was slightly higher in asthma than in emphysema. None of these differences were striking or distinctive, however, and a patient with asthma might exhibit the same abnormalities of ventilatory function, arterial blood gas composition, and pulmonary circulation as a patient with pulmonary emphysema. The one test which distinguished the two conditions was the diffusing capacity of the lung. In patients with emphysema the exercise diffusing capacity never exceeded 12.7 c.c. per minute per millimeter of mercury and was usually less than 10 c.c. per minute per millimeter of mercury. In the asthmatics, the exercise diffusing capacity was rarely less than 13 c.c. per minute per millimeter of mercury and always above 11 c.c. per minute per millimeter of mercury. This finding was interpreted as a reflection of destruction of alveolar capillaries in emphysema and the presence of a relatively normal alveolar capillary surface in asthma. E. W.

Relationship Between Pulmonary Tuberculosis and Bronchial Asthma: A Report of the Committee on Allergy. American College of Chest Physicians: Dis. Chest. **37**: 589, 1960.

After analyzing 150 patients in whom allergic bronchial asthma was associated with active or quiescent pulmonary tuberculosis, it was found that 1 per cent of patients with predominantly pulmonary tuberculosis also had bronchial asthma. An even smaller percentage of those with predominantly bronchial asthma had or had had pulmonary tuberculosis. Those patients with both diseases were adults and there was little distinction as regards sex. It was felt by the majority of the committee that neither condition had any important effect on the other. It was recommended that ACTH be given patients with severe, uncontrollable status asthmaticus even if they have active or quiescent pulmonary tuberculosis and that streptomycin and other

antibiotics be used in such cases. It was found that ACTH could be life-saving and in most cases the tuberculosis did not seem to be aggravated. Since steroids are usually given over longer periods, it is necessary to administer them more cautiously. If severe asthma persists, it is recommended that prednisone be used in association with antituberculosis therapy. E. W.

Asthma and Diabetes. Helander, E.: Acta med. scandinav. **3**: 162, 1958.

Among a series of 3,151 patients with bronchial asthma in Sweden 1.14 per cent were found to have diabetes mellitus. In a series of 3,236 patients with diabetes, at least 1.10 per cent had bronchial asthma. Thirty-six patients were found to have both diseases. These figures correspond closely with the incidence of these diseases in the general population. Diabetes is more likely to appear in asthmatics after the age of 60 years. R. W.

Effect of Smoking on Asthma and Emphysema. Peters, G. A., and Miller, R. D.: Proc. Staff Meet. Mayo Clin. **35**: 353, 1960.

Two heavy smokers, one with pulmonary emphysema and one with bronchial asthma, were studied by means of pulmonary function tests before and after they gave up smoking. After smoking had been discontinued for 9 months the emphysematous patient showed a 15 per cent increase in vital capacity and a doubled maximum breathing capacity. There was also considerable clinical improvement. After one week without smoking, the asthmatic patient showed an increase in vital capacity from 2.79 to 3.82 liters, a decrease in residual volume, and an increase in maximum breathing capacity. He had less shortness of breath and cough, and coarse rhonchi, previously present in the lungs, disappeared. These results suggest that patients with asthma or emphysema should be advised to stop smoking. M. C.

DERMATOLOGY

Phototoxicity, Photoallergy, and Photoskin Tests. Jillson, O. F., and Curwen, W. L.: Arch. Dermat. **80**: 678, 1959.

The subject of physical hypersensitivity to sunlight, with special reference to the differential diagnosis of skin reactions to sunlight, was reviewed. Phototoxicity occurs when the epidermis contains a photosensitizer and is exposed to suitable wave lengths of light. Within hours an erythematous reaction results, which has the clinical appearance of an exaggerated sunburn, persists for days and is followed by residual hyperpigmentation. A photoallergic reaction is not followed by residual hyperpigmentation, often requires an incubation period, frequently is manifested by papules or eczematoid responses, as well as urticaria, and on retesting has a markedly shortened reaction time. Photoallergic reactions, unlike phototoxic reactions, are not dependent upon specific fixed wave lengths of light. A photodynamic reaction is manifested by an urticarial response and is usually followed by hyperpigmentation, but the reaction time is not shortened by repeated exposures. Photoallergic reactions also produce urticaria but can be separated from photodynamic responses by means of the reverse passive-transfer test. If the skin is irradiated, then injected with serum from the suspected allergic patient, a positive response will only occur if it is a true photoallergic reaction. Since photodynamic substances need light and energy to be activated, the serum from such patients never produces a reaction when injected into previously irradiated skin.

In order to study more accurately the causative mechanisms in patients who manifested excessive responses from sunlight, the minimal erythema dose (MED) and the minimal delayed erythema dose (DED) were measured in patients exposed to a carbon arc lamp. The carbon arc was found to be an excellent source of a continuous spectrum of light and proved to be more reliable than exposure to quartz lamps or sunlight. Chloroquin and other antimalarial drugs were found to be most effective in preventing and relieving delayed photoallergic reactions and also helped differentiate phototoxic from photoallergic reactions. Barbiturates, sulfonamides, salicylates, and coal tar derivatives frequently induced phototoxic reactions which were manifested clinically by an exaggerated sunburn and a lowered MED. A 15 per cent concentration of PABA incorporated into a hydrophylic ointment consistently proved to be the best sunburn screen except where the sunburn was produced by wave lengths of light above 32A, which occurs in individuals sunburned through window glass or by fluorescent light. Titanium dioxide (Solar Cream) was also beneficial when PABA did not fully protect patients. Many individuals required a DED exposure to produce a photoallergic skin response. The lesions were usually papular in character and the patients invariably responded well to antimalarial therapy. Occasionally it was necessary to apply contactants to the skin and then to irradiate these sites in order to induce a contact photodermatitis. Contact photodermatitis was observed from substances such as oil of bergamot, lime oil, etc., and the reaction was diffuse in character, manifested by papular urticaria and accompanied by a mild eczematous response superimposed upon the erythema. Occasionally some patients required DED doses of erythema applied to the patch test sites before positive reactions were obtained, and frequently the responses did not become evident until several days later. Compazine, Phenergan cream, Skol, sunbath lotion, and Hazel Bishop liquid make-up were found to produce photoallergic reactions, while Thorazine, Noxzema, Cuticura ointment, Geranium, and Jergen's lotions were all shown to cause a phototoxic response. R. W.

Papular Urticaria Caused by Red Ants. Yaffee, H. S.: U. S. Armed Forces M. J. **10**: 26, 1959.

Papular urticaria caused by the red ant, Monomorium pharaonis, was reported in two patients. The first patient, a 24-year-old housewife in her third month of pregnancy, had recurrent bouts of conical papules which were extremely pruritic, lasted for three days, and then subsided with a brownish discoloration. These lesions occurred in groups for about three months. Later, this patient noted the onset of a typical urticarial papule, which followed a sharp sting by a red ant on her thigh. The use of appropriate insecticides ended the ant population of her home and the disease. The second patient, a 7-year-old child, had similar lesions which began after she played in an area of her home where red ants were seen. The child's eruptions came to an abrupt halt when her family moved from that house. E. W.

Incidence of Cutaneous Eruption Due to Sulfamethoxypyridazine. Anderson, P. C., and Wissinger, H. A.: U. S. Armed Forces M. J. **10**: 1051, 1959.

Sulfamethoxypyridazine (SMP) was administered in doses of 1 gram initially and 0.5 gram daily for seven days to 223 patients because of upper respiratory or urinary tract bacterial infections. The patients ranged in age from 15 to 70 years. All patients who had had previous unfavorable reactions to sulfa drugs or a combination of drugs with a sulfonamide were

excluded from the study. Among the patients studied, 6, or 2.7 per cent, developed cutaneous eruptions. Of these, 4 developed maculopapular rashes, 1 developed giant urticaria, and 1 patient had the sun-sensitive type of rash with purpura. In only 1 case were there any changes in the blood count. This patient's white blood count dropped to 1,200 which rapidly rose within four days of steroid therapy to normal levels. The skin lesions lasted anywhere from one to ten days. It was concluded that SMP, a potent bacterial agent which sustains adequate blood levels on small doses, was apparently a safe drug in the doses used and was recommended for further evaluation.
E. W.

Prophylaxis Against Poison Ivy Dermatitis With Parenteral Alum-Precipitated Pyridine Ivy Extract. McLoughlin, P. T.: New York J. Med. **60**: 1762, 1960.

Thirty-two individuals known to be poison ivy sensitive were patch-tested prior to and following therapy with alum-precipitated pyridine ivy extract suspended in saline. Injections were given weekly during a 10-week period, starting with a dose of 0.3 c.c. of 1:50 dilution and working up to a 1 c.c. of a 1:5 dilution. Only 17 of the 32 patients received the full course of treatment while 27 individuals received at least 8 injections. Patch tests were performed by using blotter disks previously saturated with acetone solutions of pentadecylcatechol in dilutions of 1:1000, 1:5000, and 1:10,000. Three dry saturated disks were placed on an adhesive strip which was left in contact with the individual's skin for 24 hours and read 48 hours following application. Patch-testing was repeated immediately following completion of the series of injections and again 6 weeks after the injections were stopped. All but 2 patients had at least 1 disk which changed from positive to negative. Seven patients noticed only a one disk change in sensitivity while the remaining 23 had at least a 2 disk change in sensitivity. Approximately 47 per cent of the patients became completely patch-test negative to all disks. The results suggested that 8 injections or more were needed to obtain the maximum benefit from hyposensitization. In spite of heavy exposures, only 12 of the 32 patients developed poison ivy and all but one were extremely mild cases, not even requiring medication for relief. The author suggests that immunization with an alum-precipitated pyridine ivy extract is a practical and worth-while means of preventing poison ivy. R. W.

Anaphylactoid Purpura in Children (Schönlein-Henoch Syndrome). Allen, D. M., Diamond, L. K., and Howell, D. A.: A. M. A. J. Dis. Child. **99**: 833, 1960.

One hundred and thirty-one cases of anaphylactoid purpura in children from 6 months to 16 years of age observed in a medical center over a 10-year period were analyzed. About one fourth of the patients had positive family histories for allergy. Previous personal allergic disturbances including hives, eczema, food sensitivities, and asthma had been present in 18 cases. This was considered to be only slightly above the usual incidence of major allergy in children. A specific allergen appeared to induce allergic purpura in 5 patients; of these, only one had a positive family history and previous allergic symptoms. The offending allergens included mosquito bites, wool, egg white, wheat, and milk. In the case presumed to be due to milk sensitivity, the symptoms (purpura, abdominal pain, and melena) cleared rapidly when milk was eliminated from the diet and promptly recurred when it was re-introduced. None of the other suspected offenders caused symptoms when given again. Antibiotics or drugs were not offenders. It appeared, therefore, that

specific allergens or allergic reactions to exogenous stimuli did not play a major role in the majority of patients in this study. On the other hand, about 90 per cent of the patients had evidence of infection either 1 to 3 weeks prior to or at the onset of purpura, supporting the idea that recent or concomitant infection is important in the development of the disease. Corticosteroids produced marked, immediate improvement in one third of the patients, particularly in those with edema and with gastrointestinal signs and symptoms. In another third, improvement was less dramatic though definite, and in some cases particularly those with marked renal involvement, no appreciable benefit was evident. Skin manifestations did not respond well to the steroids. Corticosteroids were not regarded as a panacea in the treatment of this disease, but were used to minimize the host reaction, suppressing the inflammatory reaction. In addition, bacterial infection was vigorously searched for and treatment with suitable antibiotics was instituted. In cases with recurrent symptoms, a search for and elimination of allergens, including food, was considered worth while. Evidence was reviewed which suggested that the origin of the syndrome might be an individual hypersensitivity phenomenon resulting in localized or widespread vascular damage. M. C.

Allergic Photocontact Dermatitis From Promethazine (Phenergan). Epstein, S.: Arch. Dermat. **81**: 175, 1960.

A 33-year-old man developed an occupational contact dermatitis of the hands which became secondarily infected. He was treated with promethazine cream and accidentally exposed his hands to sunlight following use of this preparation. Acute swelling and large blisters developed and spread beyond the area involved in the original eczematoid eruption. The photocontact dermatitis subsided quickly but the original "bartender's eczema" persisted because he continued to expose his hands to antiseptic cleaning solutions. Patch tests were made with ointments containing 1 per cent promethazine, 1 per cent promazine (Sparine), and 1 per cent chlorpromazine (Thorazine) in Neo-Base. They were applied to symmetrical sites of both upper arms and left in place for 24 hours. The sites on one arm were then irradiated for 5 minutes with long ultraviolet from the rays of a Kromayer lamp while the other patch tests served as controls. All nonirradiated patch tests were negative after 24 hours, but, after 48 hours, the patch test with promethazine became mildly erythematous and within 96 hours demonstrated a definite nonvesicular dermatitis. Nonirradiated patch tests with promethazine and chlorpromethazine remained negative. The photopatch tests with promethazine, however, within 24 hours after irradiation and 48 hours after application of the original patch, showed a vesicular dermatitis identical to the original rash on the hands. A photopatch with promazine also gave a definite response, demonstrating redness and swelling but no vesiculation. Only a mild reaction was visible from the photopatch test to Thorazine. Microscopic examination of biopsied specimens taken from the original photocontact dermatitis, the photopatch test to promethazine, and the plain patch to promazine disclosed identical responses in both the original photocontact reaction and the photopatch test to promethazine. The lesions were typical of a vesicular dermatitis with a strong eosinophilia. The author cautions against the indiscriminate use of topically applied promethazine. R. W.

ANAPHYLAXIS

Anaphylaxis in Bordetella Pertussis-Treated Mice. II. Passive Anaphylaxis With Homologous Antibody. Munoz, J., and Anacker, R. L.: J. Immunol. **83**: 50, 1959.

Experimental evidence is provided to show that fatal anaphylaxis can be induced in *B. pertussis*-treated mice by the method of passive anaphylaxis with smaller amounts of homologous (mouse) antibody than rabbit antibody and also that low concentrations of mouse antibody are more effective than rabbit antibody in sensitizing untreated mice.

The experimental animals were four strains of mice of the Swiss Webster line designated as TF, CWF, SWG and SD_2, depending on the place of origin. Rabbit antibody came from a pool of serum obtained from rabbits immunized with egg albumin (EA). Mouse antibody was produced by the intraperitoneal injection of EA and adjuvant with subsequent pooling of antibody-containing ascites fluid. Purified EA was used as the challenging antigen. The passive anaphylaxis technique consisted of intraperitoneal injection of $2x10^9$ *B. pertussis* organisms into mice followed in 4 days by intraperitoneal injection of antibody with subsequent intravenous challenge with 0.5 mg. of EA. In this way it was shown that as little as 0.012 ml. of peritoneal fluid could sensitize *B. pertussis*-treated mice to fatal anaphylaxis and the SD_{50} of *B. pertussis*-treated mice was 0.035 ml. Normal mice (untreated with *B. pertussis*) had an SD_{50} of 0.085 ml. The challenging dose was uniformly fatal in the treated group, and fatal only 50 per cent of the time in untreated controls. Mouse antibody was found to be more effective than rabbit antibody in sensitizing both *B. pertussis*-treated and untreated groups of mice. The intraperitoneal route of sensitization was equally as effective a means of sensitization as the intravenous route. Sensitivity was of longer duration in the mouse antibody sensitized *B. pertussis*-treated group than in the similarly treated group sensitized with rabbit anti-EA. The SWG and SD_2 strains of mice were found to be more resistant to passive anaphylaxis than the TF and CFW strains.

It is believed that the heightened sensitivity of *B. pertussis*-treated mice to histamine and serotonin does not enhance the sensitivity to anaphylaxis. *B. pertussis* modifies the mouse tissues and facilitates penetration of histamine and serotonin, possibly via the production of adrenal insufficiency, since adrenalectomy produces effects in mice similar to those caused by pre-treatment with *B. pertussis*. D. Stein

MISCELLANEOUS ALLERGIES

Reactions Associated With Intravenous Urography: Discussion of Mechanisms and Therapy. Hildreth, E. A., Pendergrass, H. P., Tondreau, R. L., and Ritchie, D. J.: Radiology **74**: 246, 1960.

Fatal reactions to intravenous urography have been increasing during the last three years. Among 102 urographic reactions, dyspnea occurred in 75 per cent of patients, shock in 63 per cent, cyanosis in 50 per cent, frothy sputum and pulmonary edema in 22 per cent, respiratory arrest in 14 per cent, convulsions in 12 per cent, nausea and vomiting in 10 per cent, asthma in 10 per cent, and flushing, cardiac arrest, and arrhythmia in 16 per cent. The authors classify symptoms of allergic origin into two categories, those which are severe and endanger life, and those which are mild, and consist of the immediate onset of urticaria, conjunctivitis, and rhinitis, or the delayed onset of exanthematous or urticarial eruptions. A plan is suggested for the prevention of allergic reactions. Careful consideration of the clinical history with emphasis on allergy is regarded as the most important factor in the prevention of such reactions. Since a past history or a positive family history of allergy increases the likelihood of a reaction, urography in the allergic subject should be avoided whenever possible. Skin testing with iodides is worthless in predicting reactions to contrast media. It is suggested that approximately 12 to 24 hours prior to the urographic examination, 0.1 to 0.2 c.c. of a

1:10 dilution of the preparation to be used should be injected subcutaneously. This is designed to serve as a small test dose, not as a skin test. The injection should be given in an extremity so that a tourniquet may be used to control any severe local or generalized reactions which might occur. At the time of the urographic examination, 1.0 c.c. of the contrast medium should be injected intravenously several minutes before the final injection. Minimal doses are recommended. Intravenous test doses should be administered with a three-way stopcock system connected to an intravenous infusion of 5 per cent glucose and water, to maintain patency of the needle. In case of reactions, the use of epinephrine, steroids, aminophylline, adequate airway, oxygen, cardiac stimulation and massage should be resorted to when indicated. E. W.

Fatal Glomerulonephritis Complicating Allergic Purpura Due to Chlorothiazide. Fitzgerald, E. W.: Arch. Int. Med. **105**: 305, 1960.

A 54-year-old, white man with a history of chronic cardiac decompensation, who had received frequent meralluride sodium injections as a diuretic, was switched to oral chlorothiazide therapy with excellent results. About six weeks after institution of this therapy, he developed a generalized purpuric eruption. Chlorothiazide was discontinued and within one week the purpura cleared completely. Urinalysis at this time revealed one-plus albuminuria and microscopic hematuria. Because of the recurrence of dependent edema and the apparent resolution of the purpura, the patient, without his physician's advice, resumed taking chlorothiazide. Within 24 hours after ingesting a total dose of 1 gm. of the drug, he developed a generalized purpura and shortly thereafter became disoriented and semistuporous. At this time, the blood pressure was elevated and the purpuric eruptions involved the entire body except the head and neck. Dried blood was noted in the left nostril, but funduscopic examination was negative. Basilar pulmonary râles were heard, the heart and liver were enlarged, and there was moderate pretibial pitting edema. Laboratory findings indicated a moderate anemia with a normal white, differential, and platelet count. The clotting time was nine minutes and the bleeding time one and one-half minutes. Clot retraction was within sixty minutes and prothrombin time was 100 per cent. The Rumple-Leed test was negative. Urinalysis revealed a specific gravity of 1.006, 4-plus acetone, and many red cells. The nonprotein nitrogen was 95 mg. per cent. Sulfobromophthalein retention was 36 per cent in 30 minutes and 22 per cent in 45 minutes. Intensive therapy with citrus bioflavinoid vitamin K, ascorbic acid, antihistamines, diuretics, and steroids resulted in improvement of the purpura, but the kidney function became progressively worse and the patient died.

Postmortem examination of the kidneys revealed acute diffuse glomerulonephritis of combined proliferative, exudative, and hemorrhagic types, subacute glomerulonephritis, and interstitial glomerulonephritis. Petechial hemorrhages were seen in the brain and in the myocardium. The lungs showed bilateral massive pulmonary edema. It was concluded that the underlying pathophysiology was an allergic reaction to chlorothiazide because the initial occurrence and subsequent exacerbation of the eruption were closely related to the administration of the drug. E. W.

Agranulocytosis Associated With Phenindione. A Case Report With Review of the Literature. Tashjian, A. H., and Leddy, J. P.: A. M. A. Arch. Int. Med. **105**: 121, 1960.

A 49-year-old woman with decompensated rheumatic heart disease developed a shaking chill, productive cough, and progressive dyspnea after 56

days of treatment with oral penicillin, digitalis, and phenindione. There was no family or past history of allergy. Physical examination revealed an acutely ill patient in acute cardiac failure with a rectal temperature of 103.2° F. A blood count revealed a leukopenia of 1,600 with only 1 per cent of granulocytes, and the bone marrow studies revealed that only 5 per cent of the total nucleated cells were granulocytes of greater maturity than myelocytes. The total and differential leukocyte counts eleven days after the onset of phenindione therapy had been normal. Phenindione and penicillin were discontinued and tetracycline therapy instituted. Blood and urine cultures throughout the hospital course were negative but, on the second hospital day, the patient developed stomatitis and pharyngitis. *Candida albicans* was isolated from the throat, sputum, and stool, and successful therapy was effected with nystatin. Fever subsided on the third day and there was gradual recovery from the agranulocytosis and leukopenia. On the twentieth day, a repeat bone marrow showed an abundance of mature forms in the granulocyte series and oral penicillin G was reinstituted. After discharge from the hospital, the patient continued to have normal peripheral blood counts for the following 8 months. An attempt to demonstrate phenindione-dependent leukocyte agglutinins yielded inconclusive results. No provocative oral or skin tests with drugs were attempted because of the possible life-threatening sequelae. The development of neutropenia was attributed to a hypersensitivity reaction. A review of the literature was given in considerable detail. E. W.

IMMUNOLOGY

Studies on Antibody Production by Spleen Explants Maintained In Vitro. LaVia, M. F., Uriu, S. A., and Ferguson, L. A.: J. Immunol. **84**: 48, 1960.

Antibody was synthesized in tissue culture by spleen cells of rats injected with a single intravenous dose of particulate antigen 48 to 72 hours prior to sacrifice.

Young male albino rats were immunized with one intravenous injection of formalinized, H strain, *Salmonella typhosae,* 48 to 72 hours prior to tissue culture. Sacrifice was accomplished by exsanguination via the heart and the resulting serum was tested for antibody titers. Minced splenic tissue was suspended, under aseptic conditions on a 3 μ pore-sized filter immersed in culture medium labelled with 1 μc of glycine 1-C^{14}. The system was incubated for from 48 to 72 hours in a sterile atmosphere containing a filtered mixture of 95 per cent O_2 and 5 per cent CO_2. Agitation of the culture medium was accomplished by motor-driven magnetic stirrers in each Petri dish. Controls consisted of similarly treated spleen tissue obtained from normal rats. Antibody synthesis was measured by adding the supernates from centrifuged culture medium to suspensions of the bacteria used for immunization, incubating for 30 minutes, then washing the suspension until the washings were free of radioactivity. The washed, antibody-coated organisms were then counted in a gas-flow Geiger-Mueller counter in order to measure the extent of uptake of radioactivity (antibody) from the culture medium by the typhoid bacilli (antigen). Some culture medium supernate was taken for agglutinin titration prior to processing. Pre- and post-incubation spleen-tissue fragments were examined microscopically.

Serum and tissue-homogenate extract antibody was usually absent at the time of sacrifice. After 48 to 72 hours of tissue culture, agglutinins could be detected in the culture medium from the immunized cells but not in amounts as great as those detected by the C^{14}-labelled glycine method. Cell culture material from nonimmunized control animals gave low nonspecific incorporation of radioactive glycine into antigen-bound material, whereas the amount of antigen incorporated radioactive glycine from cell culture material antibody obtained

from immunized animals was from 2 to 10 times greater. Evidence of maturation of antibody producing cells from immunized rats similar to the maturation seen in vivo during antibody production was found in histologic preparations following culture. However, the mitotic figures found in vivo were absent from the culture specimens.

The authors conclude that the synthesis of antibody which has been initiated in vivo can proceed in an in vitro system because cells which appear to originate from division of antigenically stimulated reticular cells can produce antibody during their differentiation. The amount of antibody produced depends on the number of antibody-producing cells which have divided at the time of tissue culture, or on the number of cells, capable of producing antibody, undergoing mitosis during tissue culture. D. Stein

The Cessation of Antibody Absorption in the Young Pig. Speer, V. C., Brown, H., Quinn, L., and Catron, D. V.: J. Immunol. **83**: 632, 1959.

Baby pigs are capable of absorbing *Escherichia coli* antibodies from orally ingested colostrum during early infancy.

Colostrum milk rich in anti-*E. coli* antibody obtained from sows previously immunized with a standardized *E. coli* antigen during the last trimester of pregnancy was fed to a baby pig from each of eight litters at 6-hour intervals beginning at zero hours (birth) through 36 hours of age. Blood samples were obtained from the babies prior to feeding and 12 hours thereafter and serum hemagglutination titers were determined.

The authors subjected the data obtained from the serum hemagglutination titer determinations to statistical analysis and found that absorption of colostrum antibodies was evident for several hours post partum, but absorptive efficiency declined as the animals aged. A 50 per cent reduction in absorptive ability occurred every 3 hours and beyond the age of 24 hours the absorption of antibodies from colostrum via the gastrointestinal tract was negligible. D. Stein

The Biological Activity of Soluble Antigen-Antibody Complexes. II. Physical Properties of Soluble Complexes Having Skin-Irritating Activity. Ishizaka, K., Ishizaka, T., and Campbell, D. H.: J. Exper. Med. **109**: 127, 1959.

Complexes of bovine serum albumin and its rabbit serum antibody were found to cause skin reactions in normal guinea pigs. The reactions were maximal between 15 and 30 minutes after injection. The prior intracutaneous injection of Evans blue dye was used as an indicator of local skin edema. Complexes of two antigen and one antibody molecule did not elicit skin reaction, nor did complexes formed in the region of extreme antigen excess. However, complexes formed in the region of antigen excess and containing three or more antigen and two or more antibody molecules did elicit skin reaction. Decomplementation of antiserums did not diminish the skin reaction, indicating "that complement is not necessary for the formation of active complexes *in vitro*, although the role of tissue complement in the skin reaction cannot be excluded." That the reaction is not that of passive or reversed passive cutaneous anaphylaxis was shown by a comparison of the amounts of antigen and antibody required to produce these phenomena. Reverse or direct passive skin sensitization required about 0.2 μgN of antigen and 0.75 μgN of antibody when the time interval between their injection into skin was short. The complexes under investigation contained only about 0.07 μgN of free antigen. "The threshold amount of antigen or antibody required to elicit a skin reaction when challenged as quickly as possible by the complementary reagent is in the same order of magnitude as the amount contained

in the minimum skin dose of soluble complexes." Thus, if the passive or reversed passive anaphylaxis were the mechanism of reaction the entire complex would have to dissociate and recombine in the tissues within the 2 to 4 minutes it takes to become apparent.

Pre-treatment of skin sites in the guinea pig with antigen failed to diminish the skin reactivity of subsequently injected active complexes, indicating that the toxicity of the complex is inherent in its molecular composition and is not related to re-equilibration of antigen and antibody in the tissues. The requirement that more than one antibody molecule be present in the complex is of considerable theoretic interest. E. K.

A Histologic Study of the Auto-Allergic Testis Lesion in the Guinea Pig. Waksman, B. H.: J. Exper. Med. **109**: 311, 1959.

A serial histologic study was carried out on the testis of guinea pigs injected with Freund adjuvant plus guinea pig testis material, rabbit testis, or bovine white brain matter. Immunization was carried out by a single intracutaneous injection over the sternum or a single subcutaneous injection at the nape of the neck. Immunization with guinea pig testis produced "disseminated foci of perivenous inflammation, lymphocytes and histiocytes predominating in the cellular filtrate, with invasion of epididymal, rete, and seminiferous tubules and destruction of tubular contents." Small guinea pigs were more affected than those weighing over 800 grams. The primary lesion was inflammation of testis and aspermatogenesis which was due to testicular atrophy without scarring. The earliest lesions were observed at 7 days. It is suggested that in other auto-allergies, perivenous cellular inflammation may well be the primary lesion. The architecture of the testis makes this feature particularly easy to detect.

Intercurrent infection, such as salivary gland virus infection, the production of a subcutaneous turpentine abscess, and allergic encephalitis were found to be associated with depression of seminiferous tubule function but with little or no cellular inflammation of the testis. E. K.

An Immunologic Characteristic of the Serum of Normal Pregnancy. MacLaren, J. A., Thornos, R. D., Roby, C. C., and Reid, D. E.: Am. J. Obst. & Gynec. **78**: 939, 1959.

Ouchterlony gel diffusion was carried out using as antigens sera from pregnant and nonpregnant women, and chorionic gonadotropin. Antibody consisted of serum from rabbits immunized to pregnant human serum. A serologic difference was discovered between serum from pregnant women as compared with serum from nonpregnant women. One or two precipitation lines were obtained depending on variations in technique. Antibody inhibition studies were also carried out. Chorionic gonadotropin failed to show any reaction of identity with the antigen peculiar to pregnant serum. Blood group isoagglutinins A and B also failed to alter the precipitin patterns. Beyond this, the identity of the pregnancy serum antigen remains unknown. E. K.

Studies on the Host Parasite Relationships to Schistosoma Japonicum. IV. Resistance Acquired by Infection, by Vaccination and by the Injection of Immune Serum, in Monkeys, Rabbits, and Mice. Sadun, E. H., and Lin, S. S.: J. Parasitol. **45**: 543, 1959.

Conflicting reports have appeared on the subject of immunity to *S. japonicum*. Monkeys, rabbits, and mice were found to be made resistant to

S. japonicum by a previous infestation with the same trematode. Both the number and size of the worms were reduced in the immunized animals. Worm extracts and even worm metabolites had good protective effect. Serum from infested or immunized rabbits may have conferred some degree of protection to mice (statistical probability level below 0.05). E. K.

PHARMACOLOGY, PHYSIOLOGY, AND PATHOLOGY

A Study of the Cutaneous Effects of Serotonin. Demis, D. J., Davis, M. J., and Lawler, J. C.: J. Invest. Dermat. **34**: 43, 1960.

Fifty healthy white subjects were injected intracutaneously with 0.1 ml. of various concentrations of serotonin in the form of 5-hydroxytryptamine creatinine sulfate, and the skin responses were studied. Histamine and saline were used as controls. Serotonin in concentrations of 5 to 10 μg per milliliter produced local erythema and a prominent persistent flare regularly. Cyanosis, pain, and pruritus were inconstant features of this reaction. Whealing almost never occurred, even with 200 μg of serotonin per milliliter.

The erythema induced by serotonin was completely inhibited by norepinephrine, epinephrine, neosynephrine, isoproterenol, and ergotamine tartrate and was not inhibited by reserpine, chlorpromazine, atropine, antihistamines, steroids, procaine, or iproniazid. Partial inhibition of the erythema was produced by a group of serotonin antagonists.

One of the most pronounced effects of serotonin on the human skin was constriction of large subcutaneous veins. By striping keratin away from a skin site and applying serotonin in concentrations as small as 0.5 μg per milliliter, this effect could be demonstrated. More concentrated solutions produced a greater and longer-lasting vasoconstricting effect. Attempts were made to inhibit the serotonin-induced venoconstriction with the above-mentioned agents, including the serotonin antagonists, but these were unsuccessful.

Six subjects given Evans blue dye intravenously prior to intracutaneous injections of serotonin in concentrations up to 100 μg per milliliter, failed to show evidence of increased capillary permeability. Comparative studies revealed that in order to achieve the degree of bluing produced by 1 μg per milliliter of histamine, 1,000 μg per milliliter of serotonin were required.

Thus, serotonin, despite its marked response on larger veins, lacks a significant effect on smaller vessels. The results of the above studies suggest that serotonin does not play any important direct role in whealing phenomena in human skin, although it may act indirectly. B. S.

Effect of 14-Hydroxydihydromorphinone on Respiration. Resnick, M. E., Berkowitz, R. D., Rodman, T., and Close, H. P.: J. A. M. A. **173**: 1649, 1960.

A new synthetic morphine derivative, 14-hydroxydihydromorphinone (Numorphan), was investigated for its effect upon the respiratory system. Following the performance of various pulmonary procedures on 6 normal young adults and 10 older patients with cardiovascular, pulmonary, or hepatic diseases, 1.5 mg. of the 14-hydroxydihydromorphinone (the equivalent of 15 mg. of morphine) was given subcutaneously to each of the subjects and the tests rerun after a 40-minute period. Definite depression of respiration and a marked reduction in the sensitivity of the respiratory center to carbon dioxide stimulation were observed in all 16 patients. In the 6 normal subjects, there was a reduction in the average basal minute ventilation per square meter of body surface area from 4.45 to 4.17 L., a reduction in the arterial pH

from 7.41 to 7.37 units, and an increase in arterial carbon dioxide tension from 41 to 45 mm. Hg. Similar changes were observed during the inhalation of 4.17 and 5.63 per cent carbon dioxide. The arterial oxygen saturation, respiratory rate, carbon dioxide output, oxygen uptake, respiratory quotient, basal metabolic rate, and cardiac output showed no significant change. The extent of the Numorphan effect on the respiratory center of the 6 normal subjects was shown in the marked depression (45 per cent) of the ventilatory response to changes in the carbon dioxide tension and this while there was no change in the respiratory rate and a reduction of only 6 per cent in the resting minute ventilation.

The respiratory depression was even greater in the subjects with cardiovascular, pulmonary, and hepatic diseases. Periodic breathing resembling Cheyne-Stokes respiration was observed in 5 of these 10 patients after the administration of the drug. One patient with cerebral arteriosclerosis developed apnea of 30 seconds' duration. There was a reduction in the average minute ventilation of 22 per cent, a decrease in the arterial pH of 0.05 unit and increase in the carbon dioxide tension of 6 mm. Hg. In spite of these changes, there was practically no reduction in the respiratory rate even in those patients whose minute ventilation was most severely reduced. The reduction in minute ventilation was almost completely at the expense of the tidal volume. In 7 of these 10 patients there was also a fall in the arterial oxygen saturation.

From these findings, it can be concluded that although Numorphan does not affect the respiratory rate it does cause a marked depression in the sensitivity of the respiratory center to a degree equal to that caused by an equivalent dose of morphine. Therefore, the respiratory rate is not a good guide for assessing the effect of a medication upon respiration. H. F.

6-Aminopenicillanic Acid in Urine After Oral Administration of Penicillins. English, A. R., Huang, H. T., and Sobin, B. A.: Proc. Soc. Exper. Biol. & Med. **104**: 405, 1960.

6-Aminopenicillanic acid (6-APA) is the product which is formed by hydrolytic enzymatic cleavage of the acyl side-chain from the penicillin molecule. The present study was undertaken to determine whether 6-APA could be detected in the urine of animals and man after the oral administration of penicillin G and other known penicillins. The presence or absence of 6-APA in the urine was detected by a chromatographic procedure.

When mice were fed penicillin G, 500 mg. per kilogram, 6-APA was detected in the urine within ½ hour and at 2, 6, and 24 hours. Similar findings were noted after oral administration of penicillin G to rats, cats, rabbits, dogs, and man. Only guinea pigs failed to show 6-APA in the urine after penicillin G administration. When phenoxymethyl penicillin and other types of penicillin were substituted, 6-APA was still detectable in the urine. Intravenous administration of penicillin G in mice was also followed by the urinary excretion of 6-APA. It was estimated in the mouse that only 0.1 to 1 per cent of the administered dose of penicillin G was converted to 6-APA as it appeared in the urine.

In another series of experiments, penicillin G was exposed to macerated tissue from individual animal organs in an attempt to hydrolyze it to 6-APA. These attempts failed. However, when penicillin G was added to a water suspension of intestinal tract contents of the mouse, 6-APA was detected. It is postulated that penicillin G, when given intravenously, reaches the intestinal tract via the bile, and penicillin acylase activity of the intestinal flora

forms 6-APA which is then absorbed and excreted in urine. A possible reason for the failure of penicillin conversion to 6-APA in the guinea pig is the fact that *E. coli* is almost absent from the intestinal flora in this species and gram-positive organisms are predominant. B. S.

Localization of Gamma-Globulin in the Diseased Kidney. Freedman, P., Peters, J. H., and Kark, R. M.: A. M. A. Arch. Int. Med. **105**: 524, 1960.

Sections of renal tissue from 43 patients with renal disease were studied by the fluorescent antibody technique for the presence of gamma-globulin. In 34 instances, this material was obtained by percutaneous biopsy, and in 9, it was taken postmortem as soon as possible. For control studies, renal tissue was taken from nine patients suffering from a variety of other diseases and sections from these were similarly treated. Inspection of the tissue by ultraviolet microscopy revealed either complete absence of specific fluorescence or fine streaks of fluorescence in occasional glomeruli, which in no way compared with the extent and intensity of the fluorescence seen in patients with specific renal disease. Sections from seven patients with acute glomerulonephritis revealed specific glomerular fluorescence in all cases. This took the form of a diffuse involvement of the glomerular capillary wall which appeared as a brightly staining line throughout the tuft. Fluorescent antibody studies made on two of these patients after their acute illness had subsided revealed much less gamma-globulin in the glomerular capillary wall than had been observed on the first examination in one case and a heavier deposit of gamma-globulin in the capillary wall in the second case in which clinical improvement was not marked. In two cases of proliferative glomerulonephritis, in which the only clinical symptoms were persistent albuminuria and occasional urinary casts in the sediment, the renal tissue displayed specific fluorescence which was focal within the glomerular capillary walls and of a low order of intensity. In five patients with membranous glomerulonephritis who presented the nephrotic syndrome, specific fluorescence was observed in the glomeruli in all instances. In three patients, basement-membrane thickening was mild and the fluorescence tended to be patchy within the glomerulus. In two patients with severe histologic lesions, the glomerular fluorescence was extensive and diffuse. In one patient with proliferative and membranous glomerulonephritis, whose biopsy revealed a mild, patchy thickening of the glomerular basement membrane, neither glomerular nor vascular fluorescence was observed. Sections from a patient with advanced chronic glomerulonephritis revealed well-marked fluorescence in the glomeruli, tubules, and blood vessels. Fluorescence was also seen in Bowman's capsule in some glomeruli. Diabetic nephropathy was found to be associated with extensive deposition of gamma-globulin throughout the renal cortex, involving glomeruli, tubules, and blood vessels. The glomerular capillary wall, Bowman's capsule, and the nodules all fluoresced brightly. The tubular basement membrane, tubular cytoplasm, and the walls of the small blood vessels were similarly fluorescent. Tubular casts also fluoresced. In four cases with well-marked clinical evidence of scleroderma, the glomeruli in two were found to contain gamma-globulin in the glomerular capillary wall, and in all four cases, specific fluorescence was seen in the walls of the small vessels. Renal sections from a patient with polyarteritis nodosa, whose histological examination revealed a chronic glomerulonephritis, showed the presence of gamma-globulin in many glomeruli, in the capillary wall as well as in the walls of some of the small vessels, in tubular casts, and in tubular epithelium. Fluorescent studies also revealed well-marked patches of gamma-globulin within the glomeruli of one patient

with renal amyloidosis and in the form of a patchy fluorescence in the glomerular capillary walls as well as in some of the small vessels of eight patients with systemic lupus erythematosus. It was concluded that these findings provide a limited measure of support for an immunologic reaction in the pathogenesis of some forms of glomerulonephritis and the so-called tissue diseases, the evidence for which still remains far from conclusive. E. W.

The Effect of Oxygen on the Pulmonary Artery Pressure and Lung Mechanics in a Patient With Cor Pulmonale. Bruderman, I., and Braun, K.: Harefuah **58**: 391, 1960.

A 43-year-old woman, who had a chronic cough with purulent expectoration for 18 years, was hospitalized because of signs of chronic cor pulmonale. There was a significant drop of the high pulmonary artery pressure and an increase in the lung compliance after breathing 100 per cent oxygen for 10 minutes. This indicated that the elevated pulmonary artery pressure was an important factor in decreasing the lung compliance. I. G.

Eosinophil Leukocytes and Their Reactions to Histamine and 5-Hydroxytryptamine. Archer, R. K.: J. Path. & Bact. **78**: 95, 1959.

Histamine was injected intracutaneously into ponies. Biopsies were done periodically after the injection and the specimens were examined for eosinophils. Eosinophilic response was maximal 30 hours after injection of histamine and regression was noted to base line condition in about 100 hours. There was no degranulation of cells, no evidence of extracellular eosinophilic granules, of migration of eosinophils from the injection site, or of lysis of eosinophils.

Pre-treatment of a given skin site was carried out by daily injections for 4 days, and, on the fifth day, a provocative injection was made. When pre-treatment and provocative injections consisted of histamine, biopsy showed eosinophilia of the site without edema. Histamine without pre-treatment caused both edema and eosinophilia. Pre-treatment on the same schedule with hydrocortisone or prednisolone prevented neither eosinophilia nor edema from the challenge dose of histamine. There was no evidence that these drugs lysed eosinophils. Pre-treatment with mepyramine maleate failed to antagonize the effects of histamine, although this drug, given at the same time and site as histamine, abolished both the edema and eosinophil responses. It is believed that this drug counteracts histamine only for a short time after injection and produces no lasting modification of tissue. Pre-treatment with ACTH did not inhibit the eosinophil response to histamine, although edema was decreased. Simultaneous injection of ACTH with histamine in an earlier experiment did appear to decrease eosinophil response. When histamine is released in vivo, 5-hydroxytryptamine (5-H.T.) is released. The injection intracutaneously of 5-H.T. produced slight edema but no eosinophil infiltration, and did not influence the subsequent response to histamine. Pre-treatment with histamine likewise slightly diminished the edema produced by 5-H.T. An antagonist of 5-H.T. had no effect on the cutaneous response to histamine.

It is suggested that eosinophils may have an antihistaminic effect "because the edema which would otherwise be produced by histamine is reduced or absent if histamine is injected into eosinophil-rich skin." It appears that skin rich in eosinophils is refractory to edema elicited by 5-H.T. E. K.

MISCELLANEOUS

"Wegener's Granulomatosis"—A Triad. McDonald, J. B., and Edwards, R. W.: J. A. M. A. **173**: 1205, 1960.

Wegener's granulomatosis is a clinicopathological triad characterized by necrotizing granulomatosis of the respiratory tract, a generalized vasculitis involving both arteries and veins, and focal glomerulonephritis. The condition has been considered by some authors to be a variant of the allergic vasculitides or polyarteritis but the etiological mechanism is obscure. Clinically it is characterized by intractable rhinitis, sinusitis and otitis or ocular symptoms, followed by cough and hemoptysis. Fever, joint pains, peripheral neuritis, weight loss, debility, and skin lesions of a vesicular or hemorrhagic nature are common. Terminal renal failure is caused by a focal necrotizing thrombotic glomerulonephritis.

Pathologically there is giant cell necrotizing granulomatosis involvement of the upper respiratory tract with destruction of the nasal septum, the turbinates, the bones of the paranasal sinuses, the orbit and the base of the skull. Pulmonary lesions include necrotizing giant cell granulomas of the lungs and bronchi, with circumscribed nodules and pulmonary vasculitis. Splenic involvement occurs generally with granulomas and arteritis. The condition must be distinguished from (1) Boeck's sarcoid, (2) specific infectious granulomatous diseases such as tuberculosis, syphilis, coccidioidomycosis, and histoplasmosis, (3) midline granuloma, periarteritis nodosa, and other hypersensitive vasculitides. There appears to be a common histological abnormality of "fibrinoid change" found in both Wegener's granulomatosis and the collagen diseases, which is seen in the wall of the blood vessels or in the connective tissue proper. A case report of a patient who had all the clinical features of Wegener's granulomatosis, except skin lesions, is presented. Treatment with steroids and antibiotics gave slight relief but did not affect the ultimate fatal outcome. H. F.

Evaluation of Infants Fed Soybean and Evaporated Milk Formulae From Birth to Three Months. Kay, J. L., Daeschner, C. W., Jr., and Desmond, M. M.: A. M. A. J. Dis. Child. **100**: 264, 1960.

The growth and development of 14 normal infants fed soybean formulae from birth to three months of age were compared with an equal number fed on evaporated milk formula. Thirty-two infants on an ad libitum diet were used as controls. The total weight and length gains as well as the patterns of these increases were similar in all groups. Physical examination findings and developmental achievements of these patients were similar. Hemoglobin and hematocrit values were comparable as were most plasma biochemical determinations. Total plasma cholesterol increased significantly by the age of three months in infants fed ad libitum diets, but not in the group which was fed soybean milk. A marked fall in gamma globulin occurred in all groups at three months of age. M. C.

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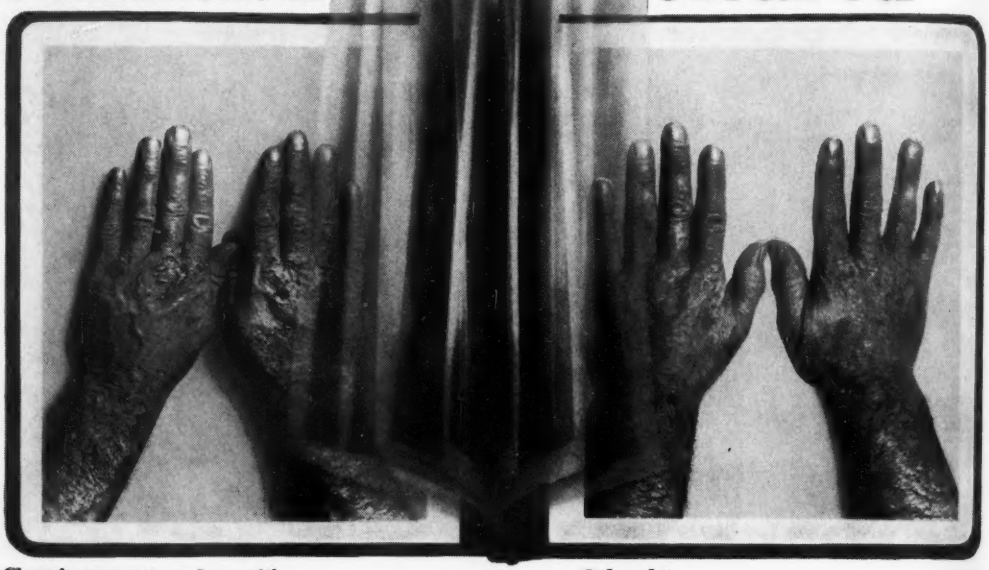

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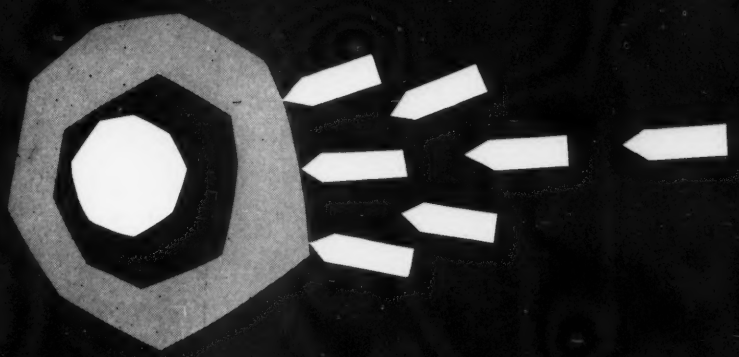

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In studies to date,[1] side effects were minimal; in a small percentage of patients, mild drowsiness was observed. Tolerance was not reported even after long usage. No cumulative effect has been observed.

Clinically proved

In studies of 459 patients,[1] Tacaryl provided effective symptomatic relief in a wide variety of conditions, including allergic rhinitis, pruritus, various skin disorders, allergic bronchial asthma, pruritus of chickenpox, and allergic conjunctivitis. In some cases, the relief of itching bordered on the dramatic.[2] In a double-blind clinical evaluation[3] of various antihistaminic agents in hay fever, Tacaryl provided benefits in all patients with moderate to severe symptoms.

dosage: *adults*—One tablet (8 mg.) or two 5 cc. teaspoonfuls syrup (8 mg.) twice daily. *children*—One-half tablet (4 mg.) or one 5 cc. teaspoonful syrup (4 mg.) twice daily.

In some cases it may be desirable to adjust dosage to meet individual requirements.

supply: Scored tablets, 8 mg., bottles of 100. Syrup, 4 mg. per 5 cc. teaspoonful, 16 oz. bottles.

references: (1) Clinical Research Division, Mead Johnson & Company. (2) Howell, C. M., Jr.: Evaluation of Methdilazine Hydrochloride as an Antipruritic Agent, North Carolina M. J. *21* (May) 1960 (in press). (3) Wahner, H. W., and Peters, C. A.: An Evaluation of Some Newer Antihistaminic Drugs Against Pollinosis, Proc. Staff Meet. Mayo Clin. *35*:161-169 (March 30) 1960.

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Symbol of service in medicine

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Allergy

Proven

in over five years of clinical use and more than 750 published clinical studies

Effective

for relief of anxiety and tension

Outstandingly Safe

- simple dosage schedule produces rapid, reliable tranquilization without unpredictable excitation
- no cumulative effects, thus no need for difficult dosage readjustments
- does not produce ataxia, change in appetite or libido
- does not produce depression, Parkinson-like symptoms, jaundice or agranulocytosis
- does not impair mental efficiency or normal behavior

Miltown®

meprobamate (Wallace)

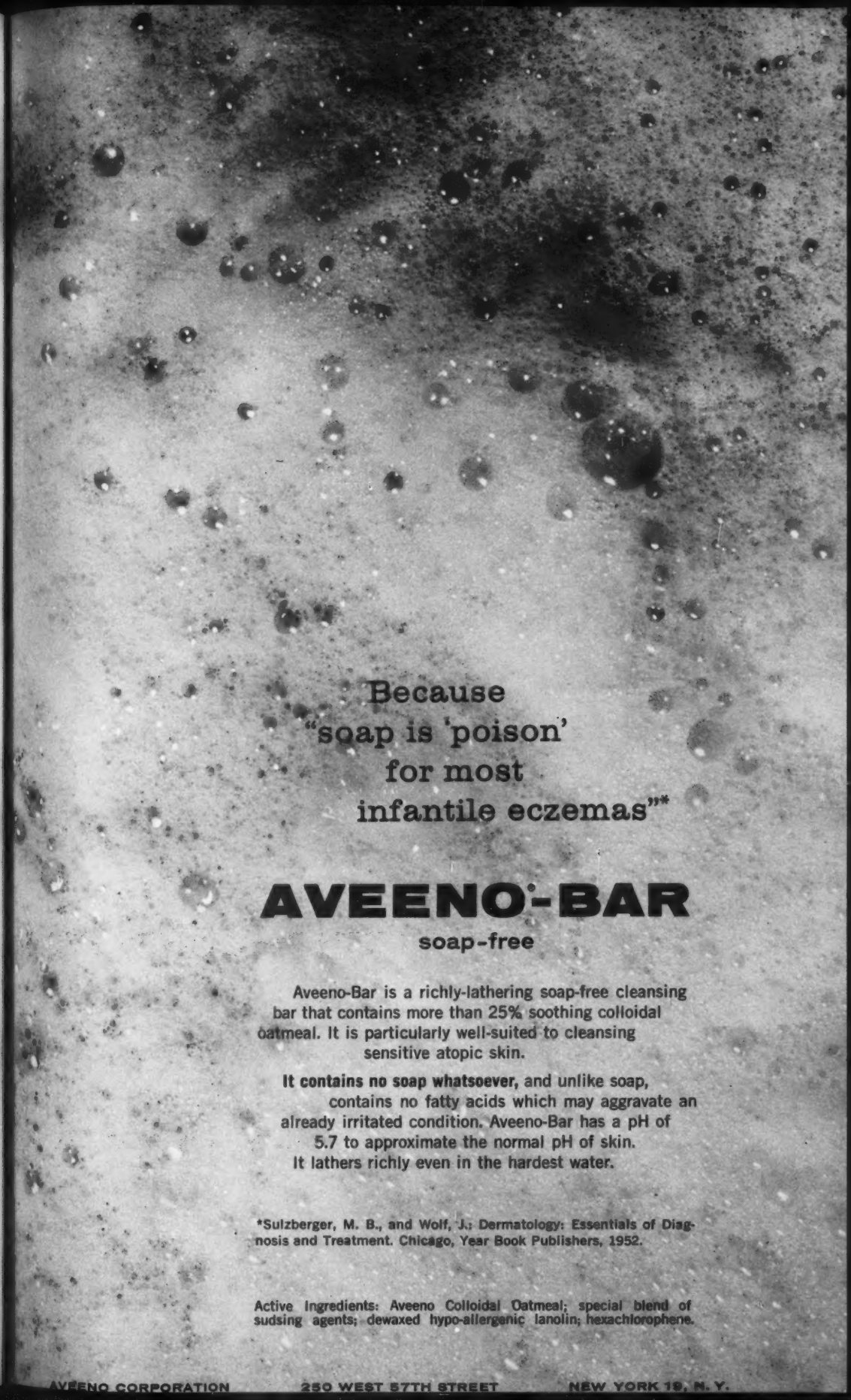
Usual dosage: One or two 400 mg. tablets t.i.d.

Supplied: 400 mg. scored tablets, 200 mg. sugar-coated tablets; or as MEPROTABS*—400 mg. *unmarked*, coated tablets.

WALLACE LABORATORIES / *Cranbury, N. J.*

GM-2058

*TRADE-MARK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"soap is 'poison'
for most
infantile eczemas"*
AVEENO®-BAR
soap-free
Aveeno-Bar is a richly-lathering soap-free cleansing bar that contains more than 25% soothing colloidal oatmeal. It is particularly well-suited to cleansing sensitive atopic skin.
It contains no soap whatsoever, and unlike soap, contains no fatty acids which may aggravate an already irritated condition. Aveeno-Bar has a pH of 5.7 to approximate the normal pH of skin. It lathers richly even in the hardest water.
*Sulzberger, M. B., and Wolf, J.: Dermatology: Essentials of Diagnosis and Treatment. Chicago, Year Book Publishers, 1952.
Active Ingredients: Aveeno Colloidal Oatmeal; special blend of sudsing agents; dewaxed hypo-allergenic lanolin; hexachlorophene.
AVEENO CORPORATION 250 WEST 57TH STREET NEW YORK 19, N. Y.

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FOR THE ACUTE STAGE

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AVEENO®
Colloidal Oatmeal
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Aveeno Colloidal Oatmeal baths have found a secure place in the therapeutic art of managing the atopic skin. They are "basic wet therapy"[2] for acute, weeping, inflamed and itching stages of infantile eczema—they are soothing, eminently safe, antipruritic and anti-inflammatory.

Available in 18 oz. and 4 lb. boxes

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"If the skin is dry, a miscible, oily preparation is added to the bath."[3]

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for **Colloidal <u>Emollient</u> Baths**

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References: 1. Epstein, N. N.: Eczema, Allergic, in Infants and Children (Atopic Dermatitis) : in Current Therapy, 1960. 2. Senear, F. E., and Haeberlin, J. B., Jr.: M. Clin. North America, March 1958. 3. Brunsting, L. A.: Postgrad. Med. 26:431, 1959.

Aveeno Corporation 250 West 57th Street New York 19, N. Y.

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INFECTED AND POTENTIALLY INFECTED DERMATOSES / PYODERMAS / ULCERS
BURNS / AFTER PLASTIC, ANORECTAL AND MINOR SURGERY

FURACIN-HC Cream combines the anti-inflammatory and antipruritic effect of hydrocortisone with the dependable antibacterial action of FURACIN®, brand of nitrofurazone—the most widely prescribed single topical antibacterial. The broad bactericidal range of FURACIN includes stubborn staphylococcal strains, and there has been no development of significant bacterial resistance after more than a dozen years of widespread clinical use. FURACIN is gentle to tissues, does not retard healing; its low sensitization rate is further minimized by the presence of hydrocortisone.

FURACIN-HC Cream is available in tubes of 5 Gm. and 20 Gm. Fine vanishing cream base, water-soluble.

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Atopic dermatitis before treatment

NOW...
to relieve inflammation fast

- mg. for mg. the most active steroid topically—up to 40 times the potency of hydrocortisone
- optimal not minimal steroid concentration for peak effectiveness... maximal contact at the site of the lesion
- stops the itch-scratch cycle to aid inflammation relief and maintain patient comfort day and night
- quick-acting broad antimicrobial activity when infection threatens recovery
- no irritating steroid particles, no sting, stain, smell, stickiness

After treatment ACTUAL CLINICAL PHOTOGRAPHS

TOPICAL CREAM

NeoDecadron*

DEXAMETHASONE 21-PHOSPHATE—NEOMYCIN SULFATE

INDICATIONS: Allergic or inflammatory dermatoses, with or without pruritus; sunburn; insect bites; otitis externa (only if the drum is intact).

CAUTION: Steroids should not be used in the presence of tuberculosis of the skin.

USUAGE: A small quantity of NeoDECADRON Topical Cream (0.1%) is applied to the affected area 2-3 times daily.

Additional information is available to physicians on request.

*NeoDECADRON and DECADRON are trademarks of Merck & Co., Inc.

Product	Steroid Concentration	ACTIVE INGREDIENTS: Dexamethasone 21-Phosphate (as disodium salt)	ACTIVE INGREDIENTS: Neomycin Sulfate	Supplied
NeoDECADRON Topical Cream	0.1%	1 mg./Gm.	5 mg./Gm. (equivalent to 3.5 mg. neomycin base)	5 Gm. (⅙ oz.) tube 15 Gm. (½ oz.) tube
DECADRON® Phosphate	0.1%	1 mg./Gm.	—	5 Gm. (⅙ oz.) tube 15 Gm. (½ oz.) tube

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Decongestant / Antihistamine

THE POTENTIATED DECONGESTANT

provides symptomatic relief of nasal congestion and rhinorrhea of allergic or infectious origin Many patients whose symptoms are inadequately controlled by decongestants or antihistamines alone respond promptly and favorably to 'ACTIFED'.

'ACTIFED' contains:	in each Tablet	in each tsp. Syrup
'Actidil'® brand Triprolidine Hydrochloride	2.5 mg.	1.25 mg.
'Sudafed'® brand Pseudoephedrine Hydrochloride	60 mg.	30 mg.

safe and effective for patients of all ages suffering from upper respiratory tract congestion

DOSAGE

	TABLETS	SYRUP (5 cc. tsp.)	
Adults and older children	1	2	three times daily
Children 4 months to 6 years of age	½	1	
Infants through 3 months	–	½	

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for "special-problem" patients...
when corticosteroid therapy is indicated

Aristocort

Lederle

surpassed "general purpose" steroid outstanding for "special purpose" therapy

in allergic respiratory disorders

Aristocort®

Triamcinolone LEDERLE

UNSURPASSED "GENERAL-PURPOSE" STEROID
OUTSTANDING FOR "SPECIAL-PURPOSE" THERAPY

ARISTOCORT Triamcinolone has long since proved its *unsurpassed efficacy and relative safety* in treating allergic respiratory disorders, including bronchial asthma. Clinical evidence has now shown that ARISTOCORT is also highly valuable for "special-problem" patients – asthmatic and others – who, because of certain complications, were hitherto considered poor candidates for corticosteroids.

for example:

PATIENTS WITH IMPENDING CARDIAC DECOMPENSATION

In contrast to most of its congeners, ARISTOCORT is not contraindicated when edema is present or when cardiac decompensation impends.[1]

PATIENTS WITH EMOTIONAL AND NERVOUS DISORDERS

Triamcinolone did not produce psychic disturbances or insomnia.[2]

PATIENTS WHOSE APPETITES SHOULD NOT BE STIMULATED

Among patients treated with ARISTOCORT, there was less appetite stimulation, especially in those who had previously gained weight on long-term therapy with other steroids.[3]

PATIENTS WITH HYPERTENSION

There was no blood pressure increase in any patient treated for bronchial asthma, and in some, blood pressure fell. Of these, three had been hypertensive.[4]

References:

1. McGavack, T. H.; Kao, K. Y. T.; Leake, D. A.; Bauer, H. G., and Berger, H. E.: *Am. J. M. Sc.* 236:720 (Dec.) 1958.
2. McGavack, T. H.: *Nebraska M. J.* 44:377 (Aug.) 1959.
3. Friedlaender, S., and Friedlaender, A. S.: *Antibiotic Med. & Clin. Ther.* 5:315 (May) 1958.
4. Sherwood, H., and Cooke, R. A.: *J. Allergy* 28:97 (March) 1957.

Precautions: Collateral hormonal effects generally associated with corticosteroids may be induced. These include Cushingoid manifestations and muscle weakness. However, sodium and potassium retention, edema, weight gain, psychic aberration and hypertension are exceedingly rare. In the treatment of allergic respiratory disorders, dosage should be individualized and kept at the lowest level needed to control symptoms. Dosage should not exceed 36 mg. daily without potassium supplementation. Drug should not be withdrawn abruptly. Contraindicated in herpes simplex and chicken pox.

Supplied: Scored tablets – 1 mg. (yellow); 2 mg. (pink); 4 mg. (white); 16 mg. (white).
Also available – syrup, parenteral and various topical forms.

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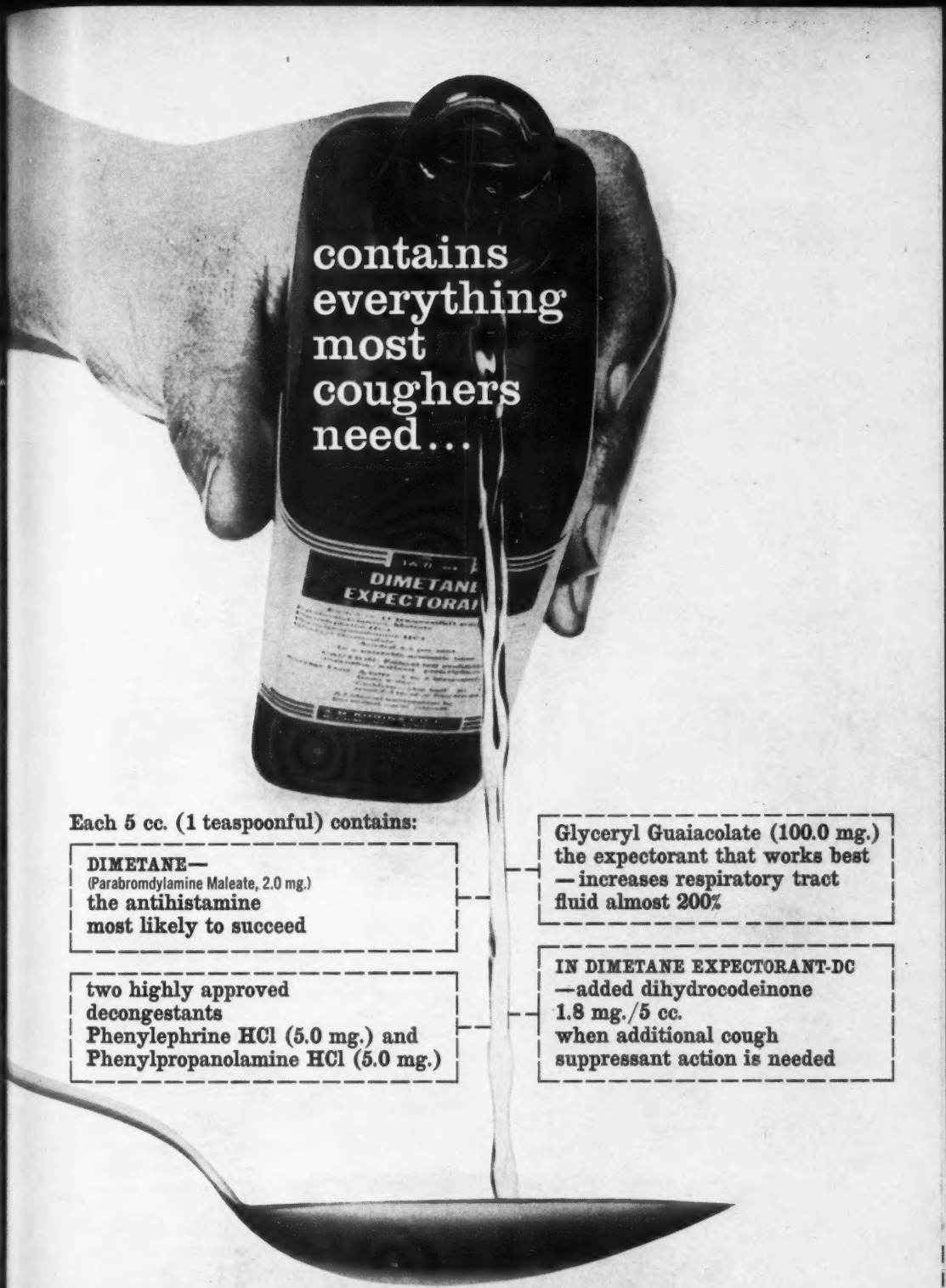

Each 5 cc. (1 teaspoonful) contains:

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(Parabromdylamine Maleate, 2.0 mg.)
the antihistamine most likely to succeed

two highly approved decongestants Phenylephrine HCl (5.0 mg.) and Phenylpropanolamine HCl (5.0 mg.)

Glyceryl Guaiacolate (100.0 mg.) the expectorant that works best —increases respiratory tract fluid almost 200%

IN DIMETANE EXPECTORANT-DC —added dihydrocodeinone 1.8 mg./5 cc. when additional cough suppressant action is needed

for less frequent, more productive cough

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DIMETANE® EXPECTORANT-DC

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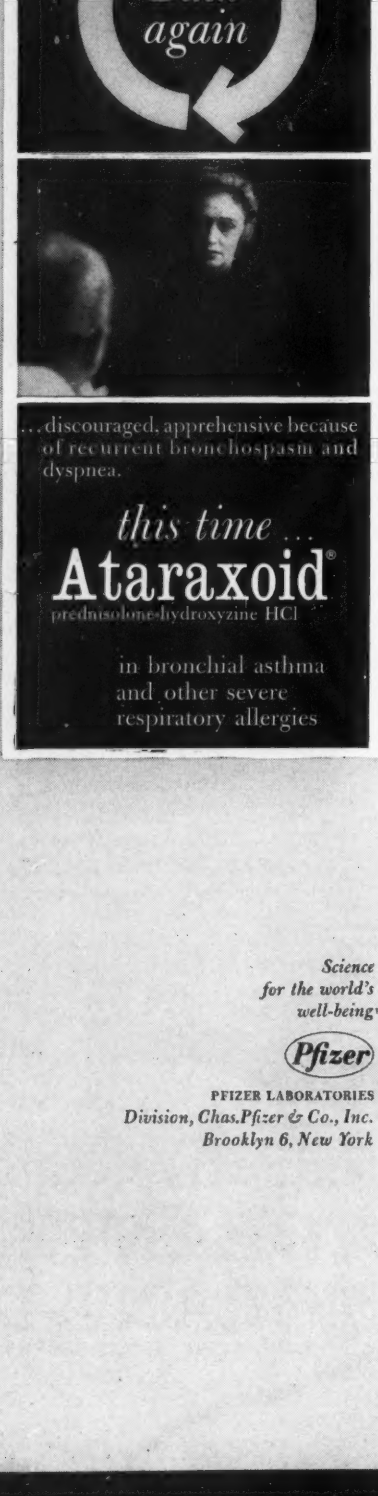
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in bronchial asthma and other severe respiratory allergies

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INDICATIONS: Allergic states, including chronic bronchial asthma and severe hay fever; rheumatoid arthritis, collagen diseases, and related conditions; other musculoskeletal disorders (myositis, fibrositis, bursitis, etc.); and allergic/inflammatory diseases of the skin and eyes.

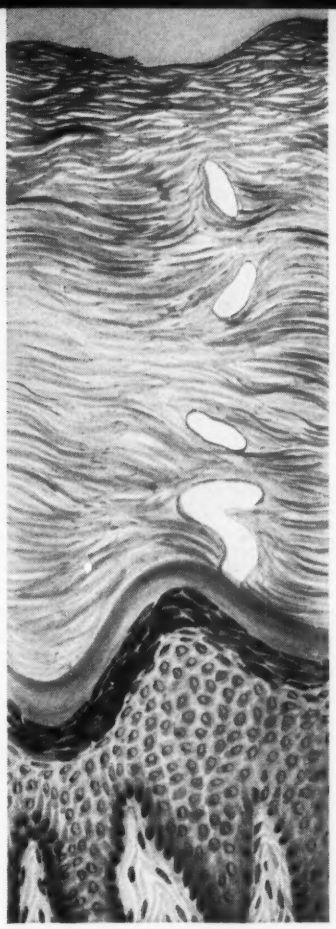
ADMINISTRATION AND DOSAGE: ATARAXOID dosage varies with individual response. Clinical experience suggests the following daily dosage: *Initial therapy*—4-6 ATARAXOID *5.0* Tablets. *Maintenance*—1-4 ATARAXOID *5.0* Tablets or 2-8 ATARAXOID *2.5* Tablets. After initial suppressive therapy, gradual reduction of prednisolone dosage should begin and continue until the smallest effective dose is reached. Prescribe in divided doses, after meals and at bedtime.

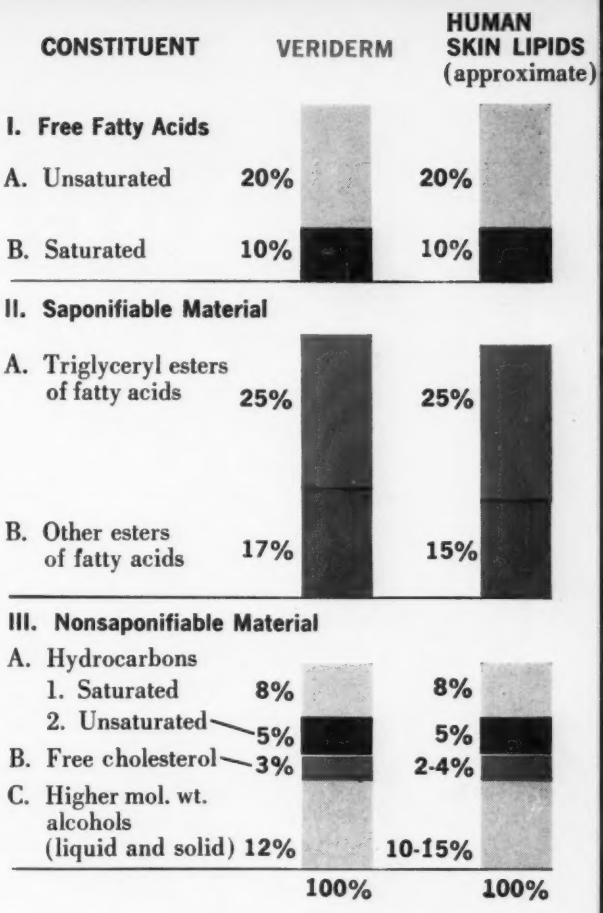
SIDE EFFECTS: Prednisolone may produce all of the side effects common to other corticosteroids. As with other corticosteroids, insomnia, mild hirsutism, moonface and sodium retention have occurred. Osteoporosis may develop after long-term corticosteroid therapy.

PRECAUTIONS AND CONTRAINDICATIONS: Usual corticoid precautions should be observed. Incidence of peptic ulcer may increase on long-term prednisolone therapy. However, therapy has often been maintained for long periods without adverse effects. Contraindicated in infectious disease including active tuberculosis (except under close supervision), peptic ulcer, certain infections of the cornea, such as dendritic keratitis, superficial punctate keratitis, epidemic keratoconjunctivitis, and in patients with emotional instability. Caution is indicated in the treatment of patients with severe cardiovascular disease, and in some cases sodium restriction and potassium supplementation must be considered.

SUPPLIED: As green, scored ATARAXOID *5.0* Tablets, containing 5 mg. prednisolone and 10 mg. hydroxyzine hydrochloride and blue, scored ATARAXOID *2.5* Tablets containing 2.5 mg. prednisolone and 10 mg. hydroxyzine hydrochloride.

More detailed professional information available on request.

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A. Unsaturated 20% 20%
B. Saturated 10% 10%
II. Saponifiable Material
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1% — Each gram contains:

Medrol (methylprednisolone) Acetate (1%)	10 mg.
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Butyl-p-hydroxybenzoate	3 mg.

1% — Each gram contains:

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Neomycin Sulfate (equivalent to 3.5 mg. neomycin base)	5 mg.
Methylparaben	4 mg.
Butyl-p-hydroxybenzoate	3 mg.

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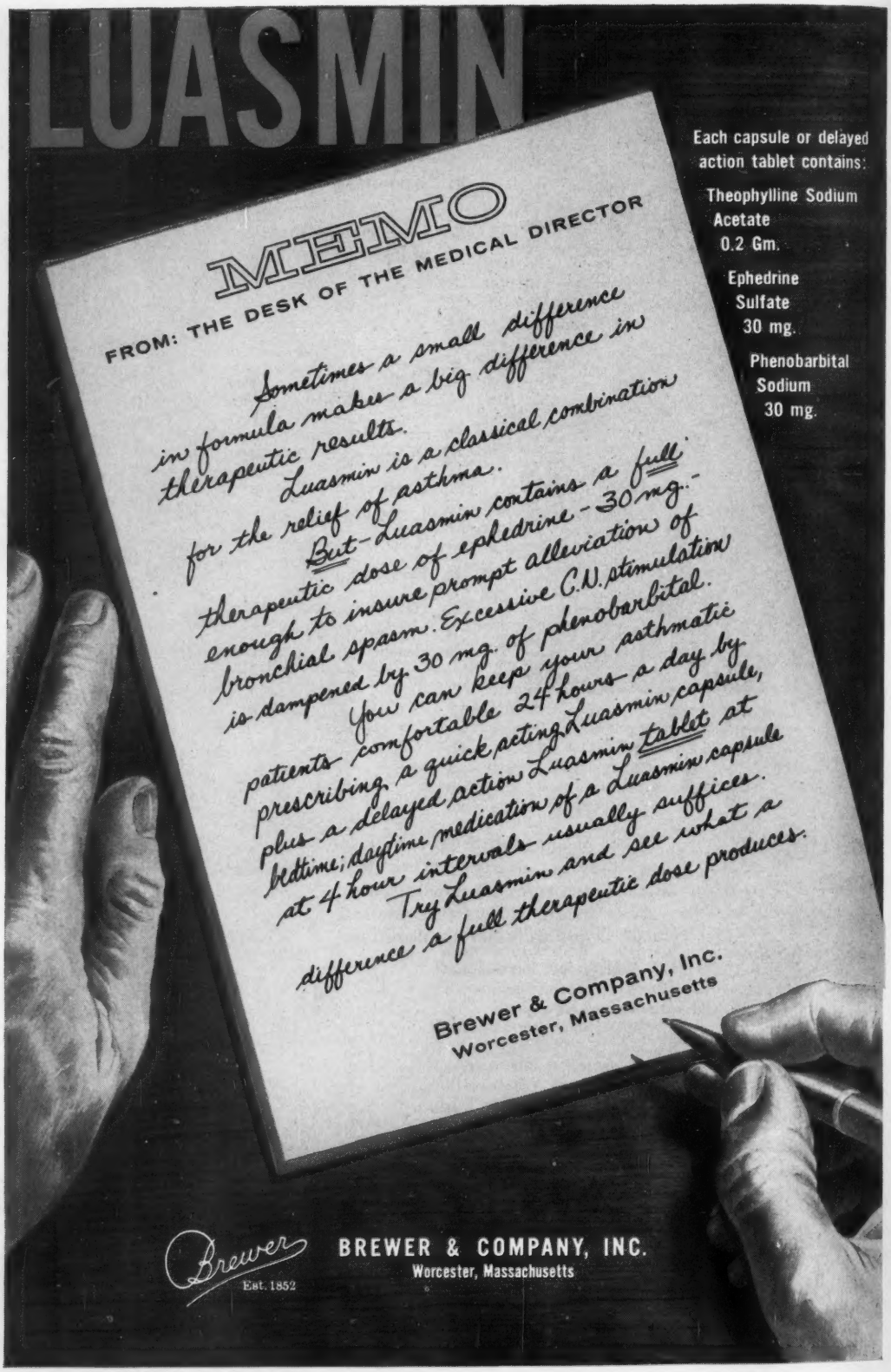
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provides simultaneous dual control of the allergic attack • *affords antihistaminic action* that relieves gastrointestinal, cutaneous, and respiratory symptoms • *exerts antispasmodic effect* for effective relief of colicky pain, nausea, and vomiting.

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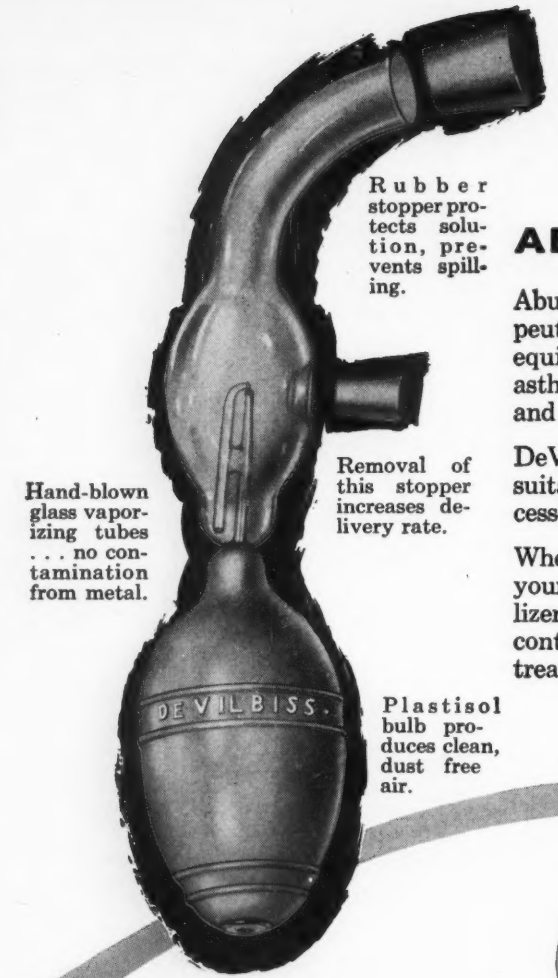

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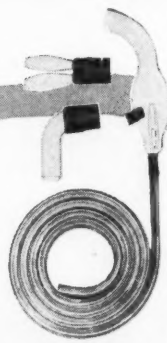

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For the Prevention and Treatment of Recurring Upper Respiratory Infections and Infectious Asthma

B.A.C.—Acellular Bacterial Antigen Complex—although derived from bacteria, is not a cellular vaccine. Prepared by the special Hoffmann process of coprecipitation, it provides the specific protective substances of the bacterial cell *plus* the toxins and metabolites. Standardized to uniform potency, B.A.C. is an acellular, water-clear solution, essentially free of sensitizing extraneous components, and is not liable to deterioration on keeping, with resultant loss of antigenic properties.

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B.A.C. combines the essential immunogenic factors for maximum immunologic response.

B.A.C. acts to improve the natural defense mechanisms—The action of B.A.C. is immunologically natural, namely, stimulation of the host's defense against bacterial invaders.

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1. Spielman, A. D.: New York J. Med. *55*:1603 (June 1) 1955.
2. Shinefield, M. A.: New York J. Med. *56*:1466 (May 1) 1956.
3. Dalven, J., and Romano, F. J.: New York J. Med. *57*:1748 (May 15) 1957.
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5. Spielman, A. D.: A.M.A. Arch. Otolaryng. *67*:204 (Feb.) 1958.

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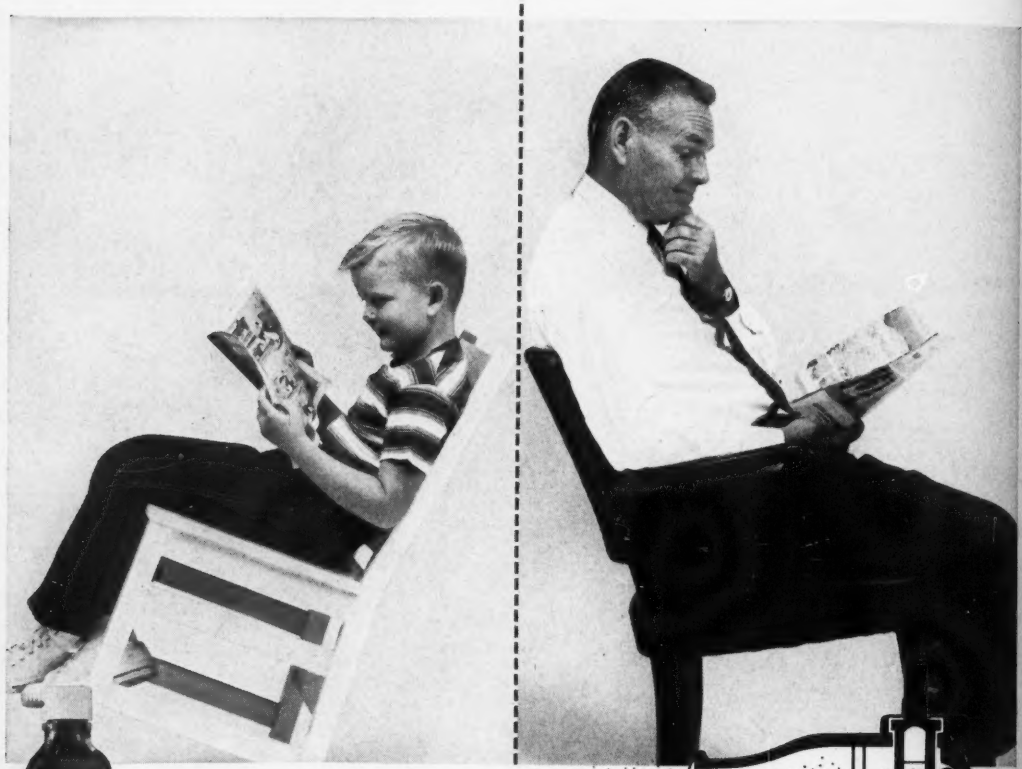
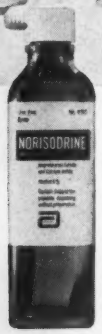
Whether it's asthmatic wheeze, sneeze, or bronchospasm... whether the patient is young or old...





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Effective in controlling allergic or bronchitic coughs, new Norisodrine Syrup also acts to prevent bronchial asthma. In relieving cough and/or wheeze, this unique kind of therapy helps to control cough-induced tension, which often will affect frequency of attacks. And, the delicate mint flavor will appeal to patients of all ages.

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stops itching...makes dry skin feel soft and smooth immediately

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ALPHA-KERI

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indicated:

as an aid in the treatment of allergic dermatoses and eczemas (contact and atopic disorders) where marked pruritus, dryness, scaling and lichenification are present.

directions:

Alpha-Keri should always be used with water . . . either added to water or rubbed into wet skin. Alpha-Keri may be used various ways. **Bath**—Add 2 to 4 capfuls to bathtub of water. Soak for 10 to 20 minutes. **Shower**—Add 2 to 4 capfuls to wet cellulose sponge. Rub gently over entire body. Rinse under shower. **Sponge Bath**—Add 2 to 4 capfuls to about a pint of warm water. Apply gently over entire body with cellulose sponge. Pat dry. **Skin Cleansing**—Rub a small amount into wet skin, rinse and pat dry.

Supplied in 8 fl. oz. bottles.

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Mask of the Husk Face Society of the Iroquois Indians, made of braided corn husk. Masks such as these were important for their symbolism and not their beauty.

Courtesy of The American Museum of Natural History.

NEO-DILODERM™

Schering

dichlorisone acetate with **neomycin** sulfate

specialized for the skin–economized for the patient
for dermatoses responsive to topical steroid therapy

- TERMINATES ITCHING
- CURBS INFLAMMATION
- FACILITATES HEALING
- ECONOMICAL
- EFFECTIVE AT VERY LOW STRENGTH
- PROLONGED IN ACTION
- NEOMYCIN PROTECTS AGAINST INFECTION

available with or without neomycin as–

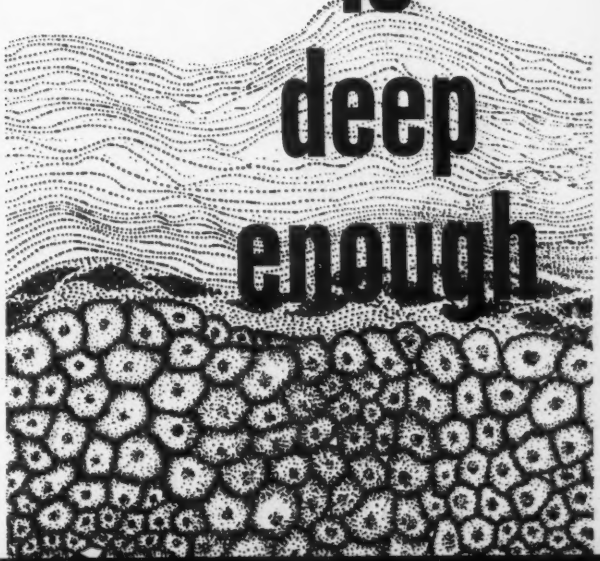
Foam Aerosol, 10 Gm. dispenser, 18.75 mg. dichlorisone acetate or 18.75 dichlorisone acetate with 37.5 mg. neomycin sulfate (equivalent to 26.25 mg. neomycin base);

Aerosol, 50 Gm. container, 8.33 mg. dichlorisone acetate or 8.33 mg. dichlorisone acetate with 16.6 mg. neomycin sulfate;

Cream, 5 Gm. tube, 2.5 mg./Gm. dichlorisone acetate or 2.5 mg./Gm. dichlorisone acetate with 5 mg./Gm. neomycin sulfate (equivalent to 3.5 mg./Gm. neomycin base).

S-693

skin deep is deep enough



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Center LABORATORIES INC.
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Complete Allergy Service - From Solution to Syringe

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(1) Silbert, N. E., Ciba Clinical Symposia; 6: 86: May 1954
(2) Mechaneck, I., Annals of Allergy; 12: 164: March 1954
(3) Rosen, F. L., J. Med. Soc. N.J.; 51: 110: March 1954

FOR ASTHMA, EMPHYSEMA, CHRONIC BRONCHITIS

INSPIRED RELIEF IN SECONDS[1]

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A TEXTBOOK THERAPY FOR ASTHMA

Just 3 to 6 inhalations of Vaponefrin relieve bronchospasm and restore breathing comfort

"...the greatest improvement (in vital capacity-time relationship) occurs during the first second."[1]

Unsurpassed record of efficacy and safety
Vaponefrin Solution (racemic epinephrine)...

- "The preparation we have found most effective is called 'Vaponefrin'."[3]
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- Its exclusive baffle produces a voluminous mist of particles with average radii of 1 micron.[1]
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References:

1. Segal, M. S., and Dulfano, M. J.: Chronic Pulmonary Emphysema, New York, Grune & Stratton, 1953, p. 99. 2. Farber, S. M., and Wilson, R. H. L.: Ann. Int. Med. 50:1241, 1959. 3. Barach, A. L., and Cromwell, H. A.: Med. Clin. No. America, May 1940, p. 621. 4. Bickerman, H. A., and Barach, A. L.: Drugs of Choice, 1960-1961 (W. Modell, ed.), St. Louis, The C. V. Mosby Co., 1960, p. 524.

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1.) Stoughton, R. B.: Report To The Council; Steroid Therapy In Skin Disorders, J.A.M.A. 170:1311-1315 (July 11) 1959. 2.) Goodman, H.: Concentration of Topical Medications Dispersed in Evaporating Vehicles with Particular Reference to Hydrocortisone Alcohol, Clin. Med. 6:781-784 (May) 1959.

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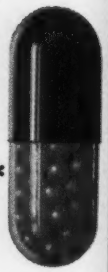

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pH-patterned slow release...

not here at pH 1.2

In the relatively acid medium of the fasting stomach, Medules are kept essentially intact by their special pH-sensitive coating (about 5% of Medrol content released in 2 hours at pH 1.2).

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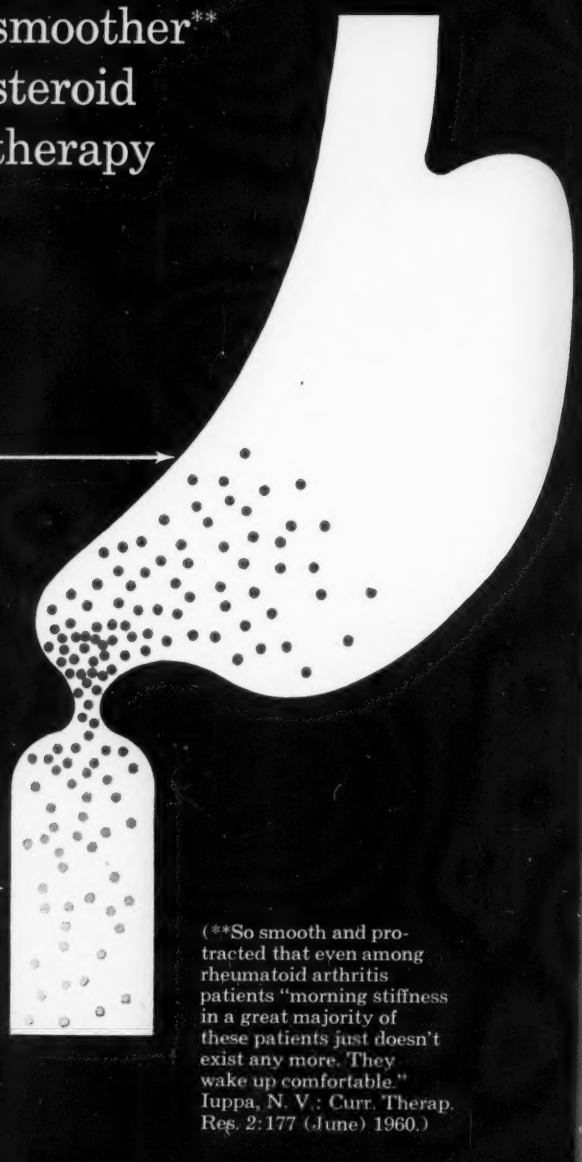
In the environment of the duodenum (at pH of approximately 7.5) 90% to 100% of the Medrol content is released within 4 hours.

135 tiny doses mean smoother** steroid therapy



(**So smooth and protracted that even among rheumatoid arthritis patients "morning stiffness in a great majority of these patients just doesn't exist any more. They wake up comfortable." Iuppa, N. V.: Curr. Therap. Res. 2:177 (June) 1960.)

...means gradual steroid absorption

Medrol hits the disease, but spares the patient

*Trademark, Reg. U.S.P. methylprednisolone

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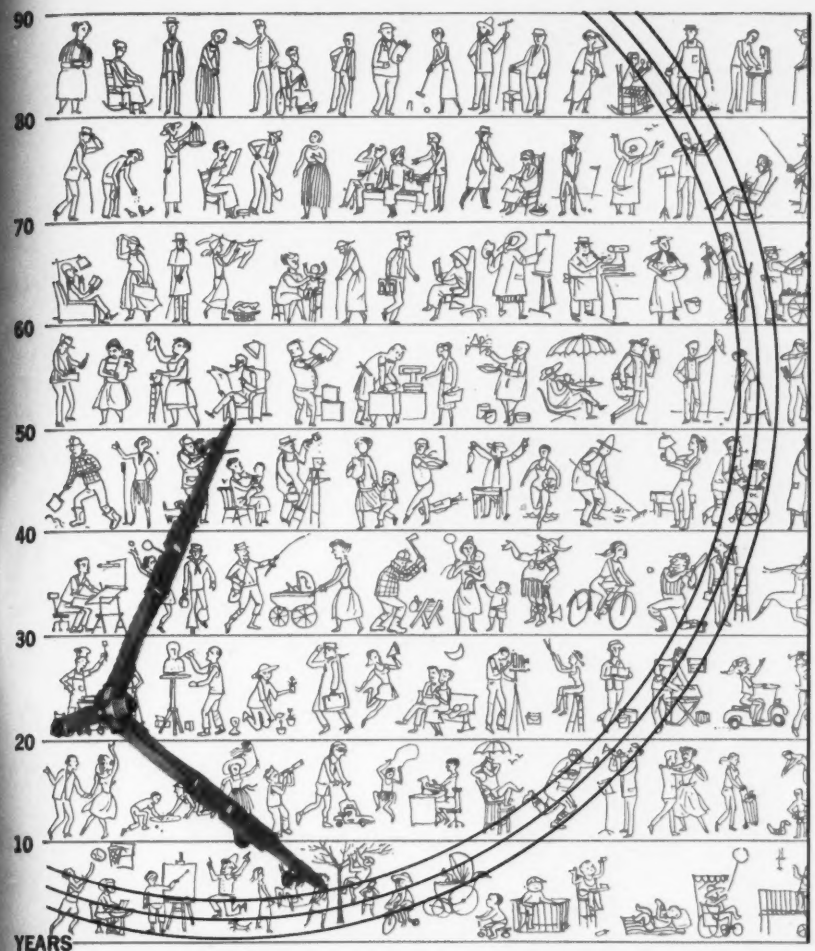

senile anxiety
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hostility
irritability
apprehension
hysteria
insomnia
chronic urticaria
alcoholism
menopausal syndrome
neuro-dermatoses
functional gastrointestinal disorders
psychoneuroses
tension headaches
dysmenorrhea
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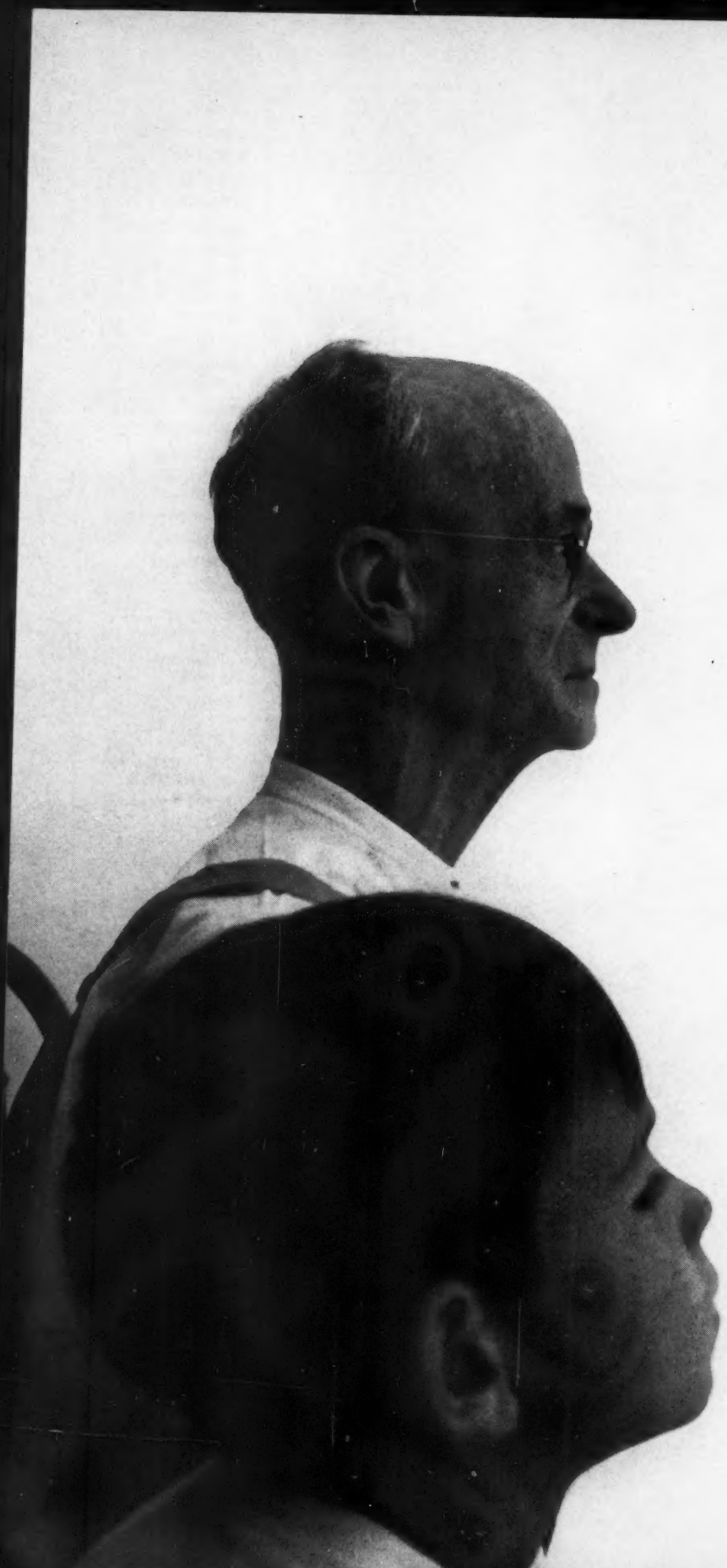

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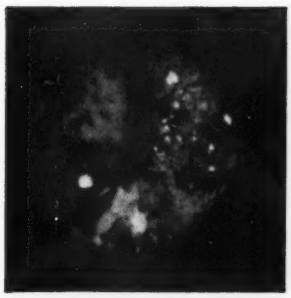
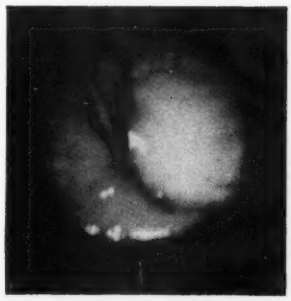
The Upjohn Company, Kalamazoo, Michigan **Upjohn**

Excellent results in ulcerative colitis even where other steroids have failed

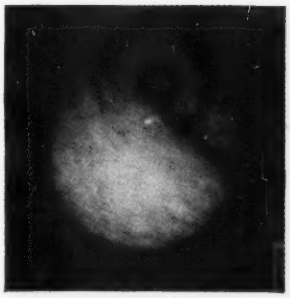
Proctoscopic view of the sigmoid in acute stage of ulcerative colitis



Proctoscopic view of the sigmoid following Depo-Medrol retention enemas for acute stage of ulcerative colitis



Proctoscopic view of sigmoid colon in a normal person



In controlling ulcerative colitis (recurrent, moderately severe, severe, and resistant), Depo-Medrol† can be given topically (by enema or rectal instillation) in requisitely large doses without producing significant side effects. Excellent results are obtainable even where other steroids have failed and improvement continues on oral Medrol maintenance dosage.

there is only one methylprednisolone, and that is

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the corticosteroid that hits the disease, but spares the patient

Medrol is supplied as 4 mg. tablets in bottles of 30, 100 and 500; as 2 mg. tablets in bottles of 30 and 100; and as 16 mg. tablets in bottles of 50. Depo-Medrol is supplied as 40 mg. per cc. injectable suspension in 1 cc. and 5 cc. vials. Mode of administration: Depo-Medrol (40-120 mg.) given as retention enema or by continuous drip three to seven times weekly.

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sets a new standard in portable air cleaners

Honeywell scientists have developed a portable electrostatic precipitator based on the same principles as their commercial units now operating in hospitals, offices and industrial buildings. It promises more effective relief from dust, pollen, bacteria, soot, smoke and other airborne contaminants than had been possible with a portable.

The new Honeywell Portable Electronic Air Cleaner will remove dirt particles as small as .01 microns (1/2,500,000 of an inch). This figure is based on research tests using the National Bureau of Standards Dust Spot Method. The same tests prove it will remove an average of 90%* of all airborne contaminants.

It will handle 150 cubic feet of air a minute* to clean a closed 12′ x 14′ room in less than 15 minutes. Just as important is its *clean air factor*—(efficiency times air flow). The Honeywell Portable Air Cleaner has a *clean air factor* of 135*. We invite you to compare this figure with that of any other unit presently available.

**Slightly less with charcoal filter.*

price $229.95
Includes activated charcoal filter

Ozone production is low, the concentration in the room is less than .01 parts per million. The lowest published figure for safe exposure in an eight-hour day is 0.1 parts per million.

Smoke and odors, of course, complicate airborne irritation. The new Honeywell Portable includes an activated charcoal filter that removes virtually all gases and odors. In appearance it resembles a piece of lightweight luggage. It can easily be carried from room to room, and plugged into any wall outlet.

Designed to deliver the maximum efficiency possible, the Honeywell Portable Electronic Air Cleaner is necessarily more expensive than other portables. A product of Honeywell's research laboratories, it is backed by Honeywell service staffs in over 112 cities, and fully guaranteed. It is now available at selected department stores, physician and office supply dealers. For a detailed analysis and specifications, write Honeywell, Dept. JL-11-130, Minneapolis 8, Minnesota.

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Same chemical proved effective in hospital use against Staphylococcus 80/81, now adapted for first time to home use by allergy patients. Added to mop or wash water, can be used on washable walls, floors, woodwork, in closets, basements, garbage cans—wherever mold, fungus and decay are problems. The lowly household mop is a great spreader of molds. However mops and wash cloths used in Bye Mold become mold and fungus free. Pint bottle, $3.95, makes 16 gallons of solution.

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ALLERGY FREE PRODUCTS FOR THE HOME

A complete line of products for the control of dusts and airborne irritants in the home.

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NEW . . . *The Finest Air Purifier On The Market Today . . .*

HONEYWELL ELECTRONIC AIR FILTER INCLUDES CHARCOAL FILTER

Nearly 100% efficient in daily use tests against dust, pollen, smoke, other airborne irritants. Quality construction means higher price of course—but well worth it for your patients who can afford the extra money. For any size room. $229.95.

Each air purifier sold by us must meet our standards: its effectiveness must be proved by tests—not by advertising claims, and its purchase must be justified on merit alone—not bargain price. Each unit completely portable—can be used with air conditioner. Every unit COMPLETELY TESTED BEFORE SHIPPING FASTEST WAY.

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PORTABLE "101"—Manufactured by McGraw-Edison. Comes with permanent electrostatic filter and ultra-violet lamp. A durable unit, and your patients will appreciate its low price. For small rooms. $39.95.

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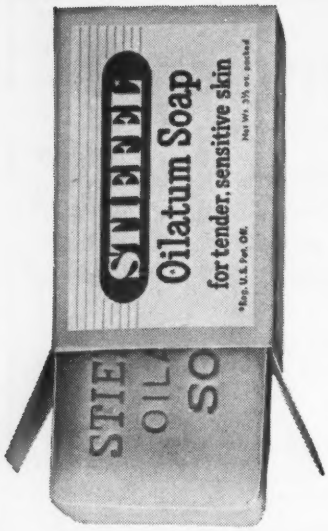

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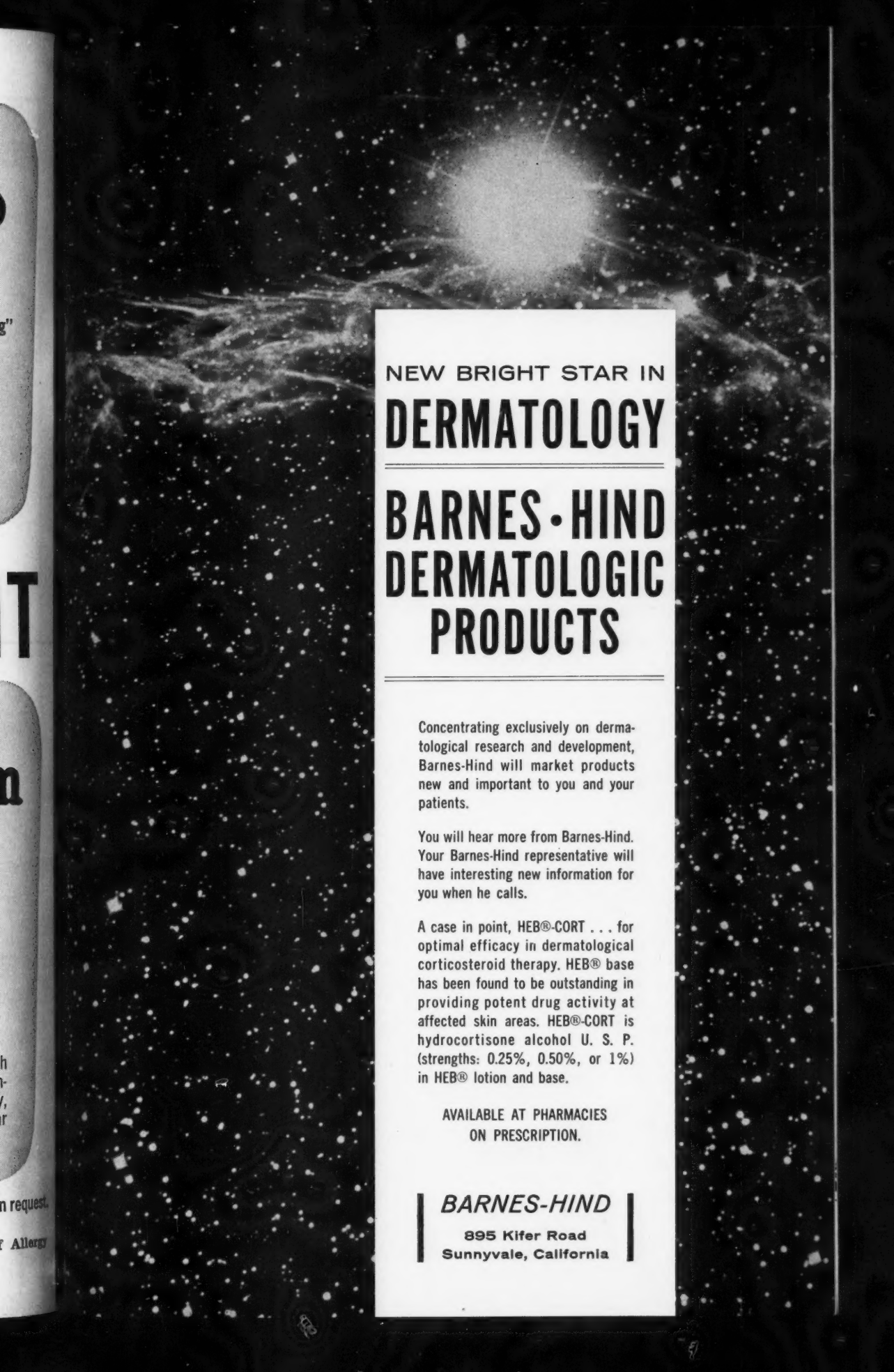
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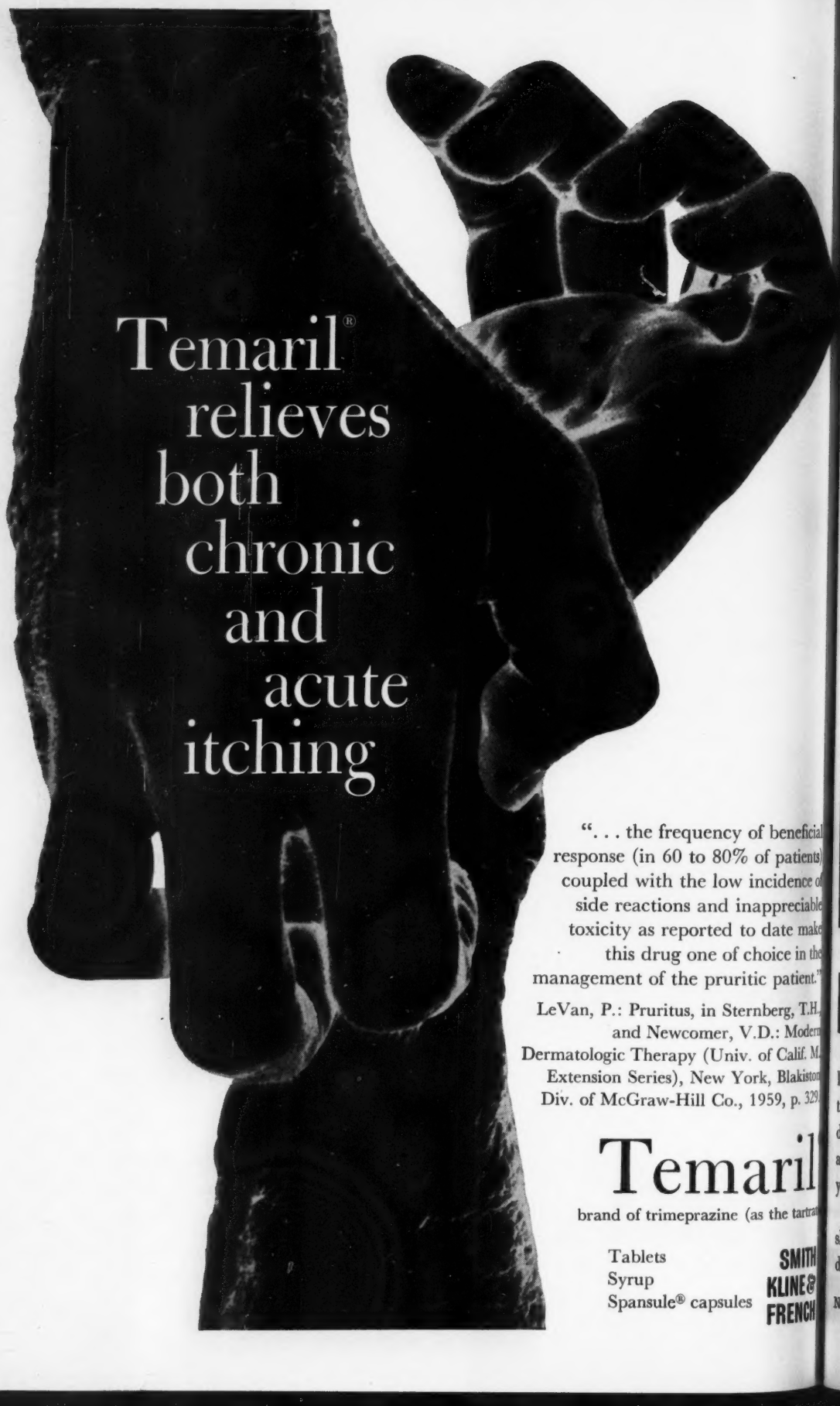

". . . the frequency of beneficial response (in 60 to 80% of patients) coupled with the low incidence of side reactions and inappreciable toxicity as reported to date make this drug one of choice in the management of the pruritic patient."

LeVan, P.: Pruritus, in Sternberg, T.H., and Newcomer, V.D.: Modern Dermatologic Therapy (Univ. of Calif. M. Extension Series), New York, Blakiston Div. of McGraw-Hill Co., 1959, p. 329.

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brand of trimeprazine (as the tartrate)

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Syrup
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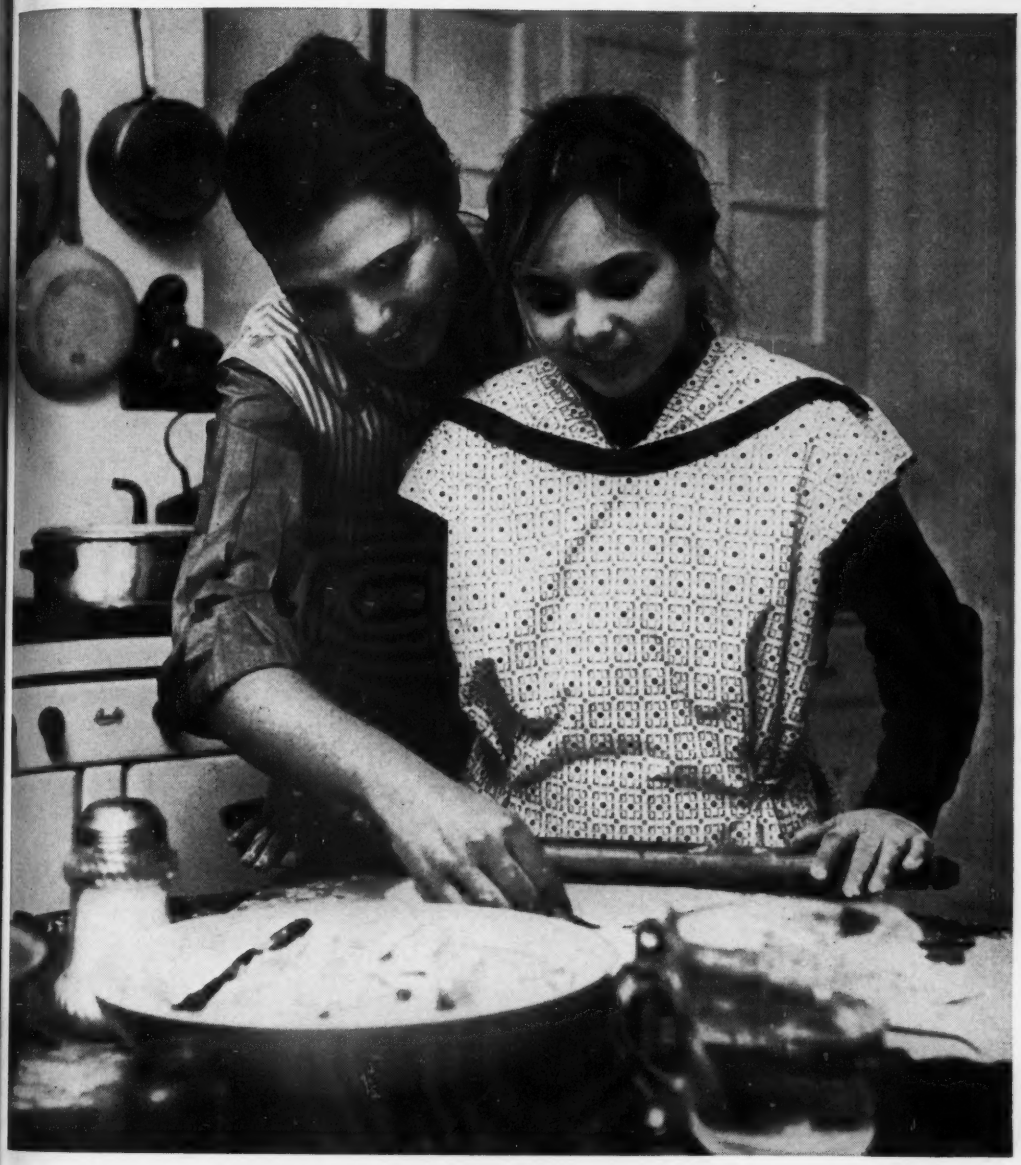

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for equanimity without somnolence

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beauty without tears

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NEW AR-EX HYPO-ALLERGENIC

Now from the laboratories of AR-EX comes a complete line of hypo-allergenic eye beauty aids. Tests have proved that women sensitive to usual eye cosmetics can safely use AR-EX Hypo-Allergenic Eye Make-Up. In a glamorous array of fashion-fresh shades.

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Brāsivol is supplied in 3 abrasive grades, permitting gradual intensification of abrasive action as the acne improves. Also, Brāsivol Base (abrasive free) now available for acute inflammatory cases.

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REFERENCES:
SAPERSTEIN, R. B.: Treatment of Acne with Long Term Continuous Abrasion. Presented at 107th Annual Meeting of A.M.A.
REES, R. B.; BENNETT, J. H.; GREENLEE, M. R.: Newer Drug Treatment in Dermatology, Cal. Med.; 91:1, July 1959.
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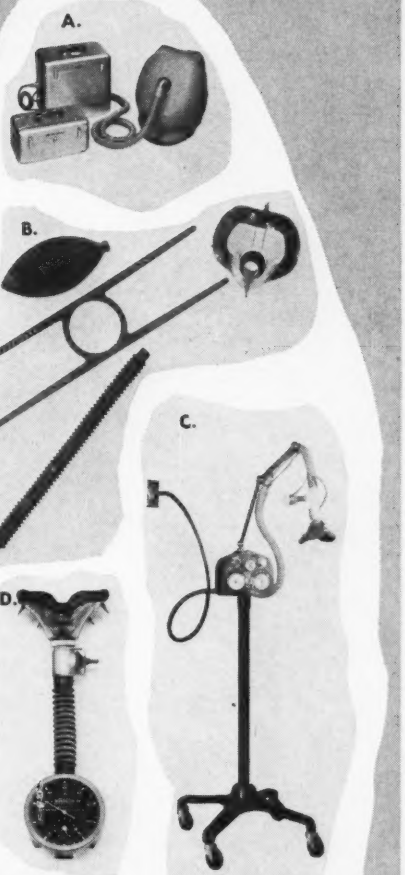

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Rogers, H.L.: Postgrad. Med. *26*:85 (July) 1959.

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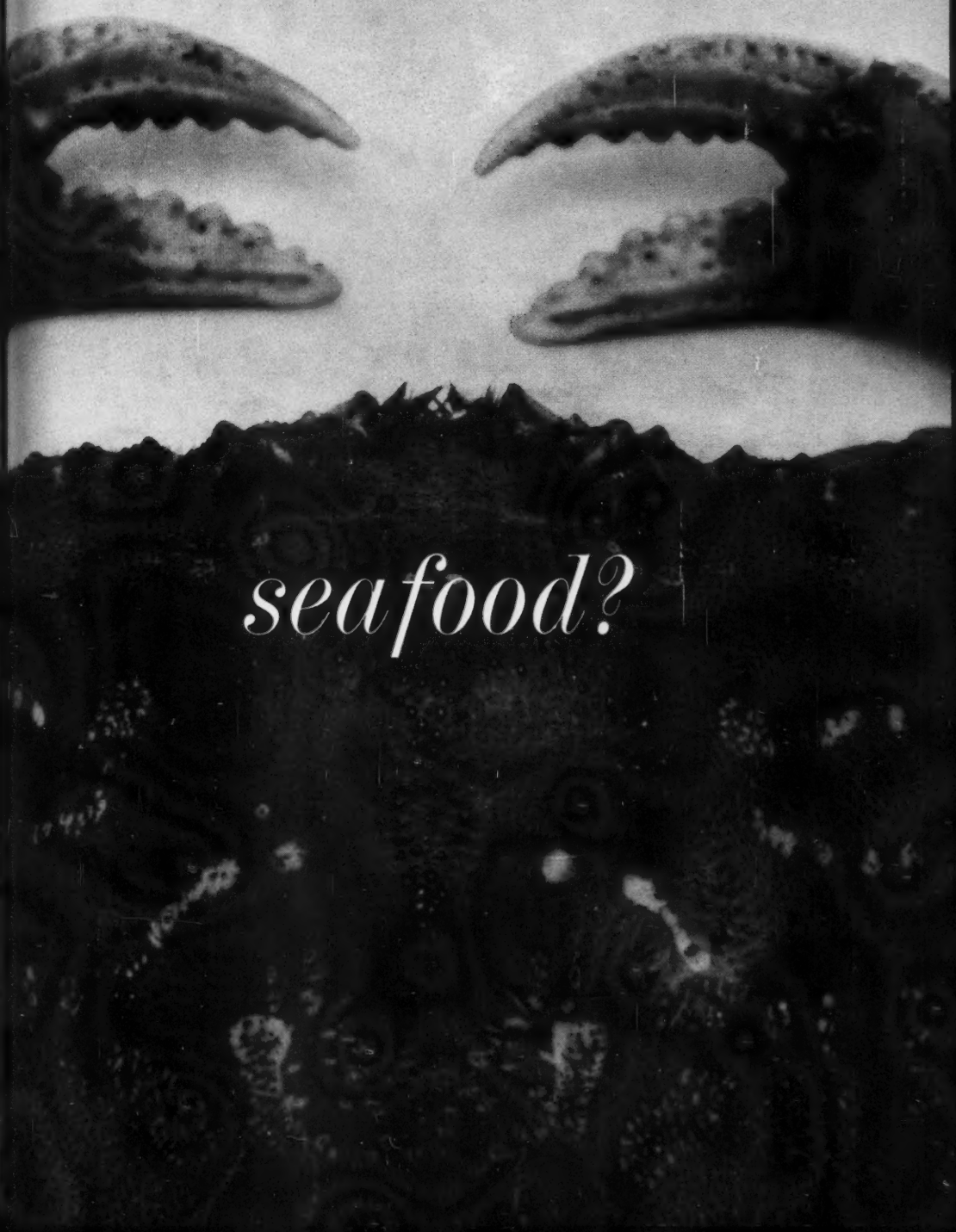

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1. Schluger, J. et al.: Am. J. Med. Sci. 233:296, 1957.
2. Bradwell, E. K.: Acta med. scand. 146:123, 1953.
3. Truitt, E. B. et al.: J. Pharm. Exp. Ther. 100:309, 1950.

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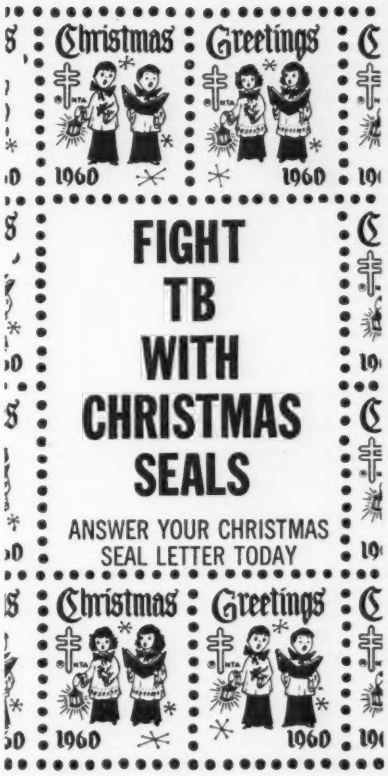

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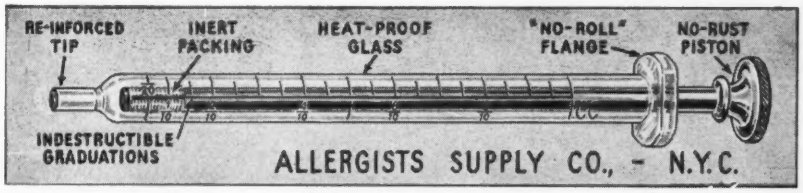

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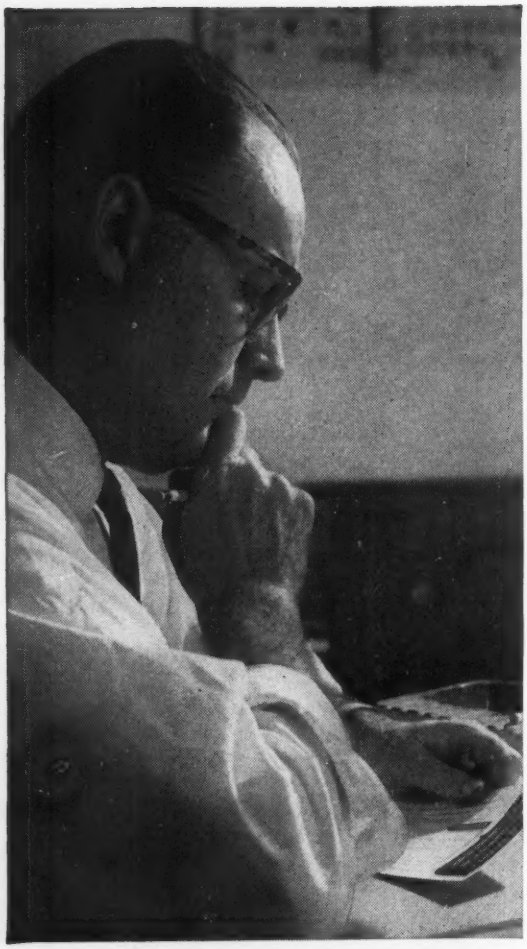

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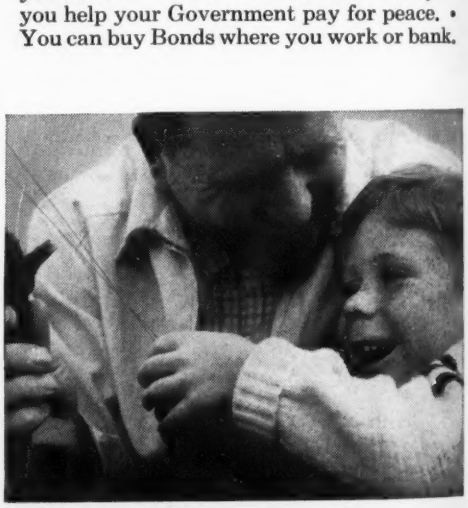

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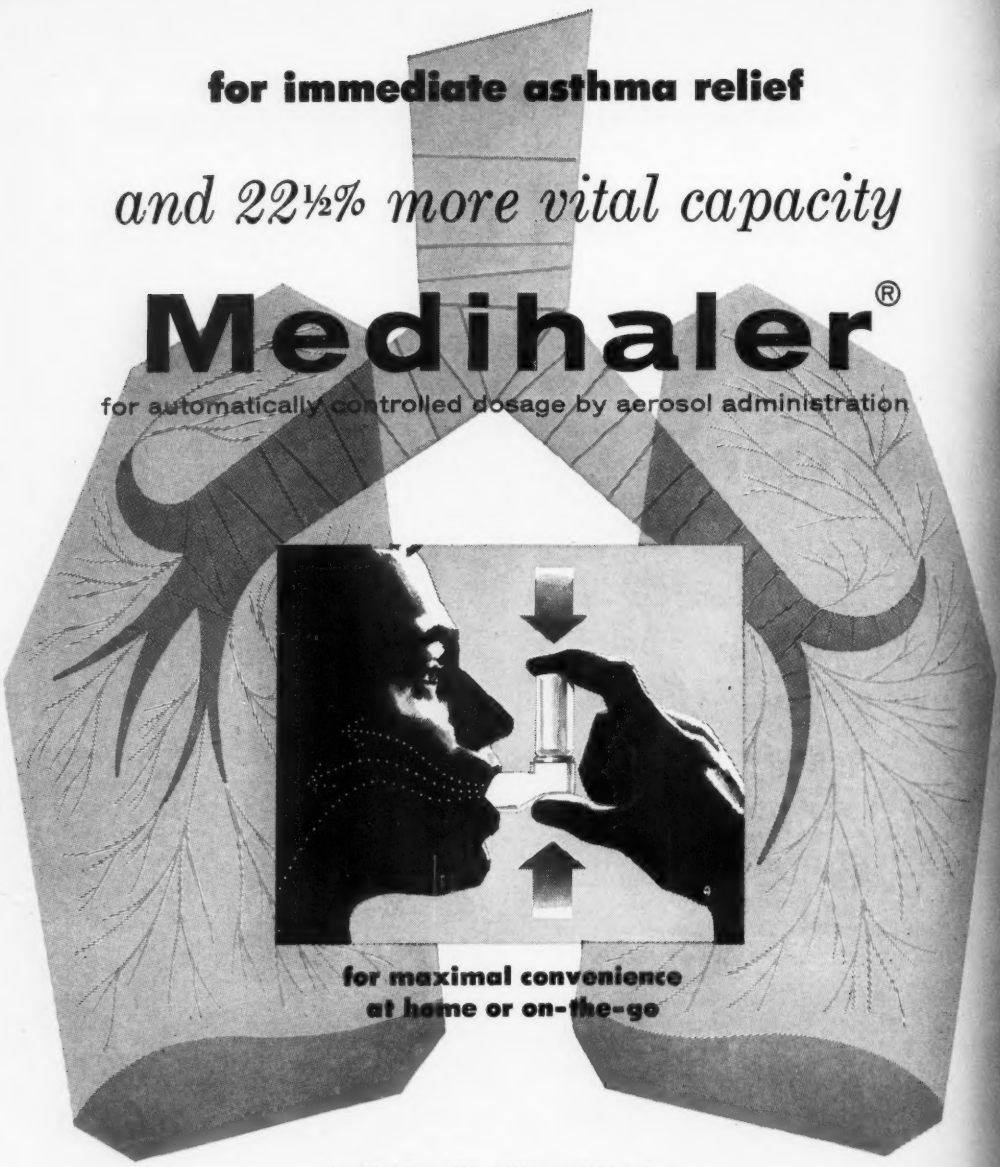

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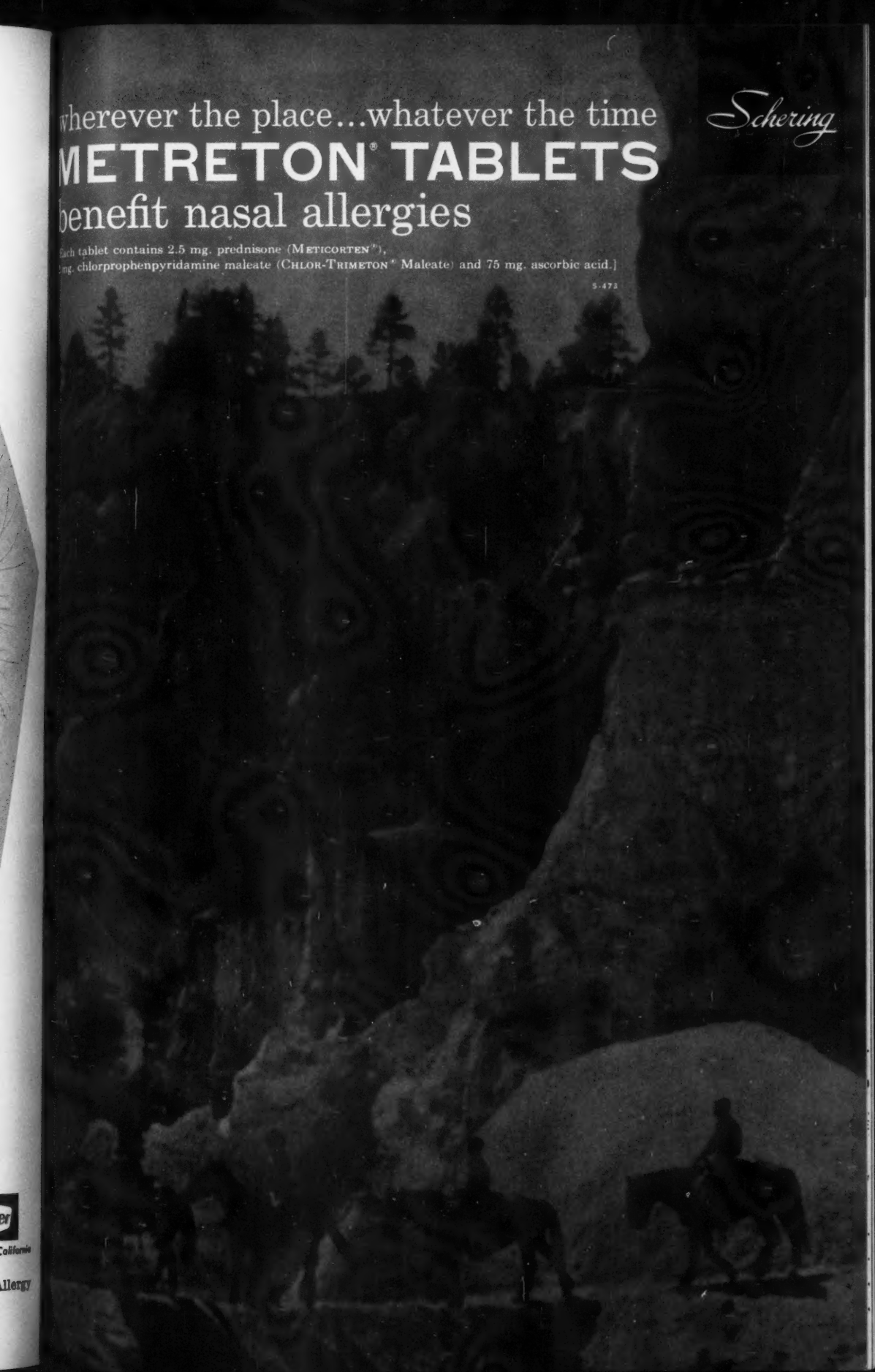
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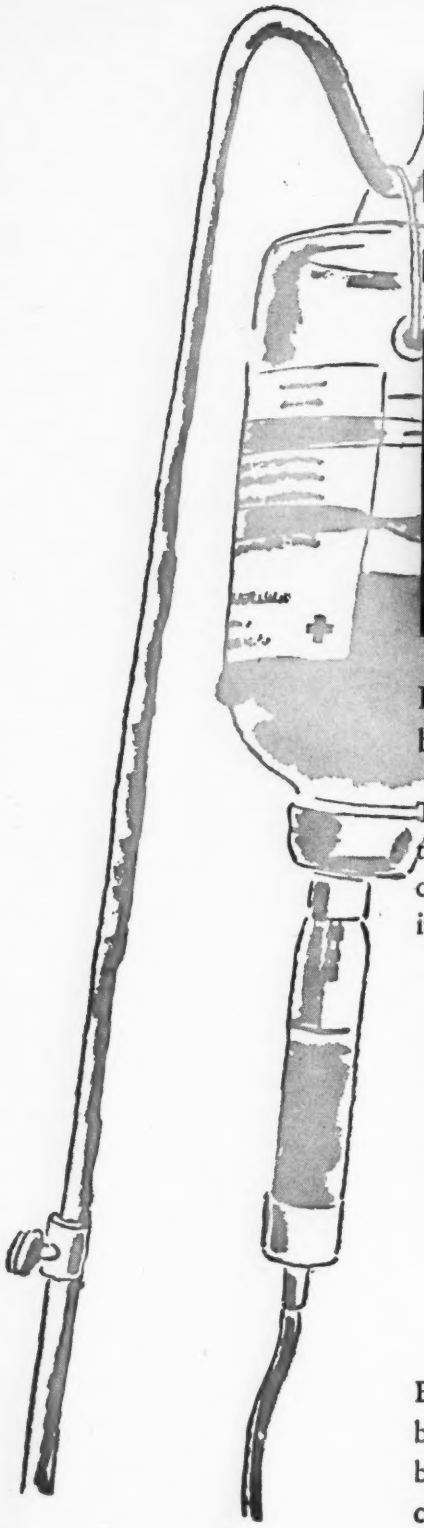

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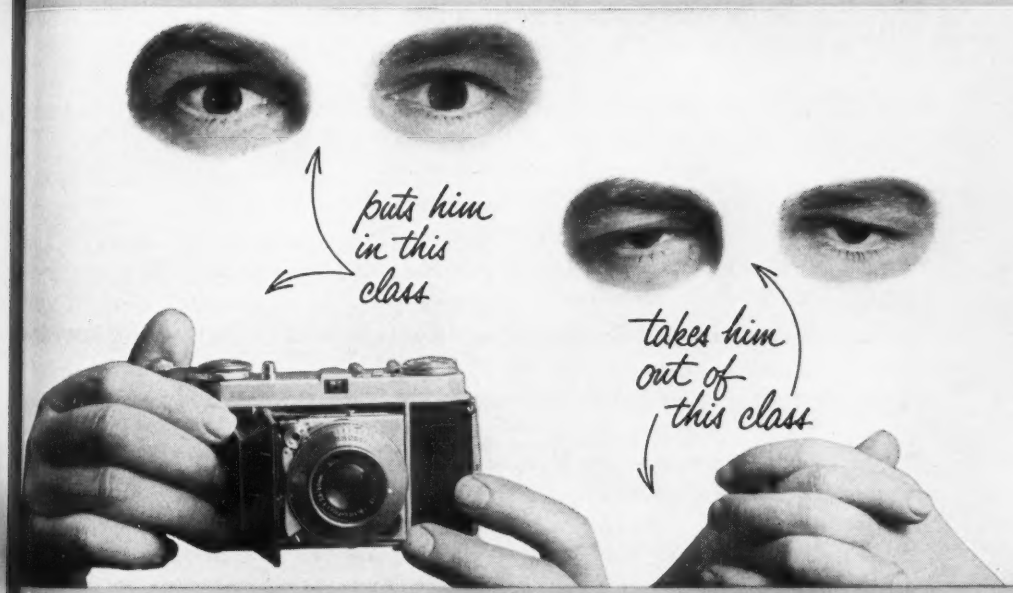

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This is another example of how the medical profession and the American Cancer Society can cooperate in essential public education in the fight against cancer.

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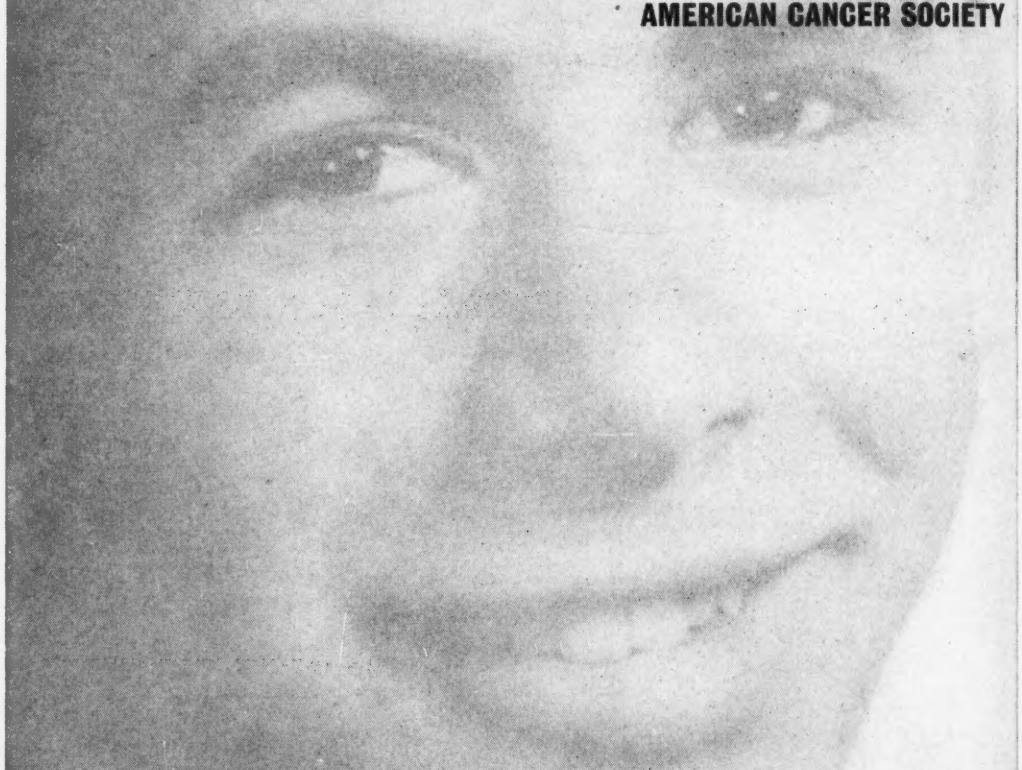

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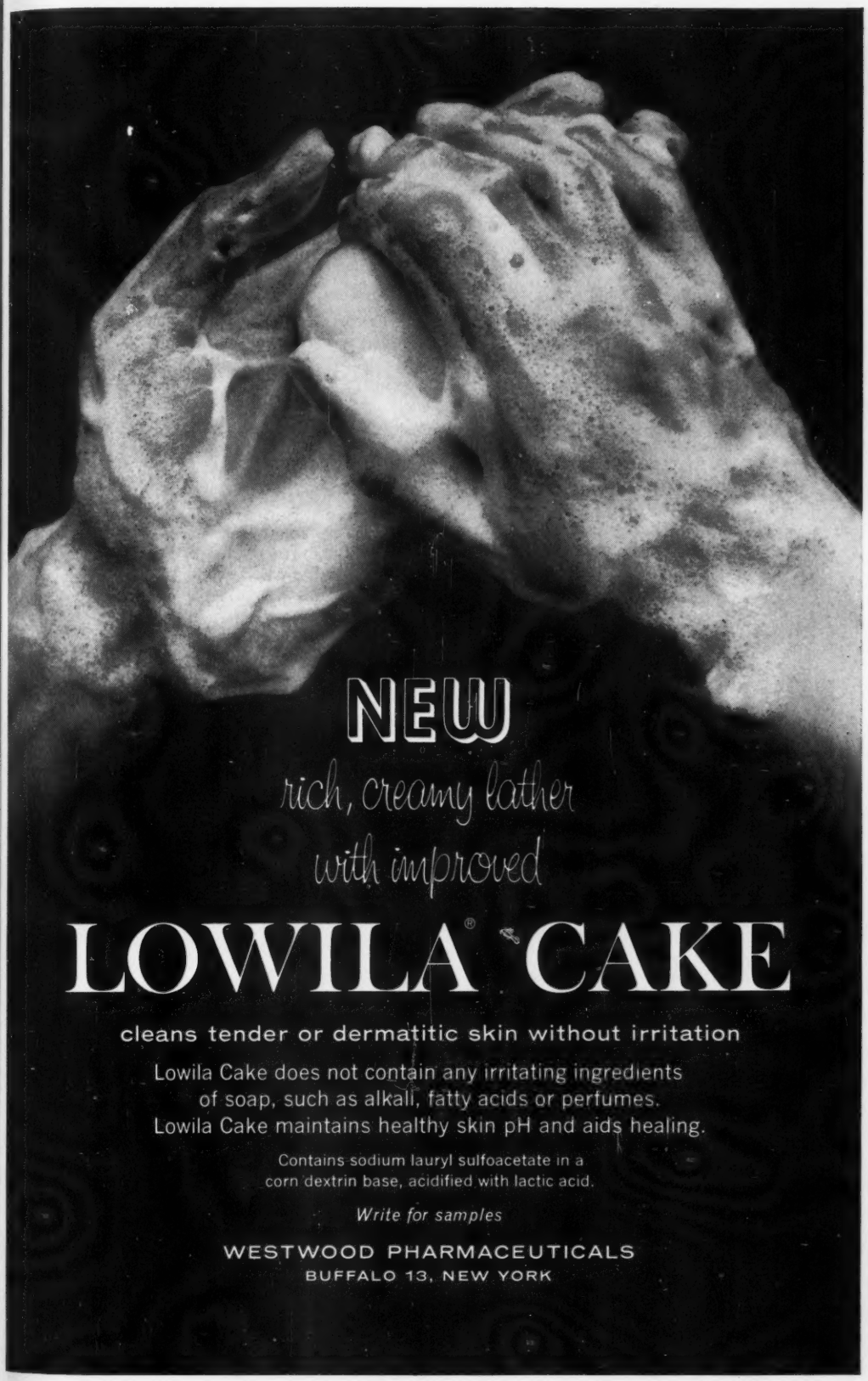
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